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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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CONTENTS

Original Communications

Society of University Surgeons

Technical Considerations in Surgical Therapy For Coarctation of the Aorta. Robert E. Gross, M.D., Boston, Mass. ---- 1

Arteriovenous Fistulas and Arterial Aneurysms in Military Personnel. Lieutenant Colonel Harris B. Shumacker, Jr., and Major Kenneth L. Carter, Medical Corps, Army of the United States ---- 9

Certain Aspects of Battle Wounds of the Thoracic Cavity. Julian Johnson, M.D., D.Sc. (Medicine), Philadelphia, Pa. ---- 26

Alterations of the Blood Following Intrathoracic Operations. Louis B. Thomas, M.D., W. E. Adams, M.D., and Thomas F. Thornton, Jr., M.D., Chicago, Ill. 38

Experimental Appendical Peritonitis. I. The Prognostic Significance of Certain ------Hematologic Factors Especially the Prothrombin Time. John Howard Kay, M.D., and John Salem Lockwood, M.D., New Haven, Conn. ---- 56

Neoplastic Biliary Obstruction. Clarence Dennis, M.D., and Richard L. Varco, M.D., Minneapolis, Minn. ---- 72

Experiences With the Pauchet Technique of Colostomy Closure. Lieutenant Colonel George Benton Sanders and Lieutenant Colonel Philip H. Halperin, Medical Corps, Army of the United States ---- 82

The Treatment of Patients With Achalasia by Esophagogastrostomy. K. S. Grimson, M.D., R. J. Reeves, M.D., J. C. Trent, M.D., and A. D. Wilson, M.D., Durham, N. C. ---- 94

The Treatment of Cardiospasm by Esophagogastrostomy. H. Glenn Bell, M.D., San Francisco, Calif. ---- 104

Transplantation of Toes For Fingers. Forrest Young, M.D., Rochester, N. Y. -- 117

Clinical and Experimental Observations on the Use of Gelatin Sponge or Foam. Hilger Perry Jenkins, M.D., Rudolph Janda, M.D., and James Clarke, M.D., Chicago, Ill. ---- 124

Multicentric Origin of Intraoral Carcinoma. Danely P. Slaughter, M.D., Chicago, Ill. ---- 133

Penicillin-Phthalylsulfathiazole Antagonism. Edgar J. Poth, M.D., Ph.D., Robert I. Wise, Ph.D., and Mary P. Slattery, B.S., Galveston, Texas ---- 147

Differential Spinal Block. Stanley J. Sarnoff, M.D., and Julia G. Arrowood, M.D., Boston, Mass. ---- 150

Review of Recent Meetings

Annual Meeting of the Society of University Surgeons. Clarence Dennis, M.D., Minneapolis, Minn. ---- 160

Book Reviews

Book Reviews ---- 162

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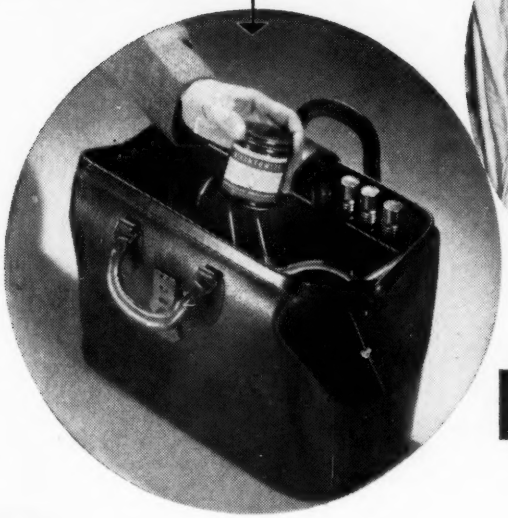

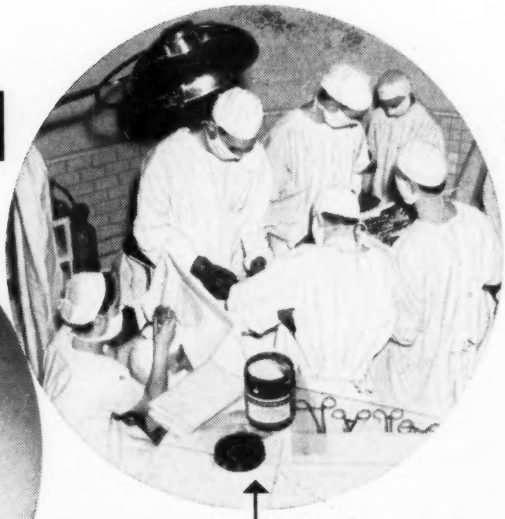

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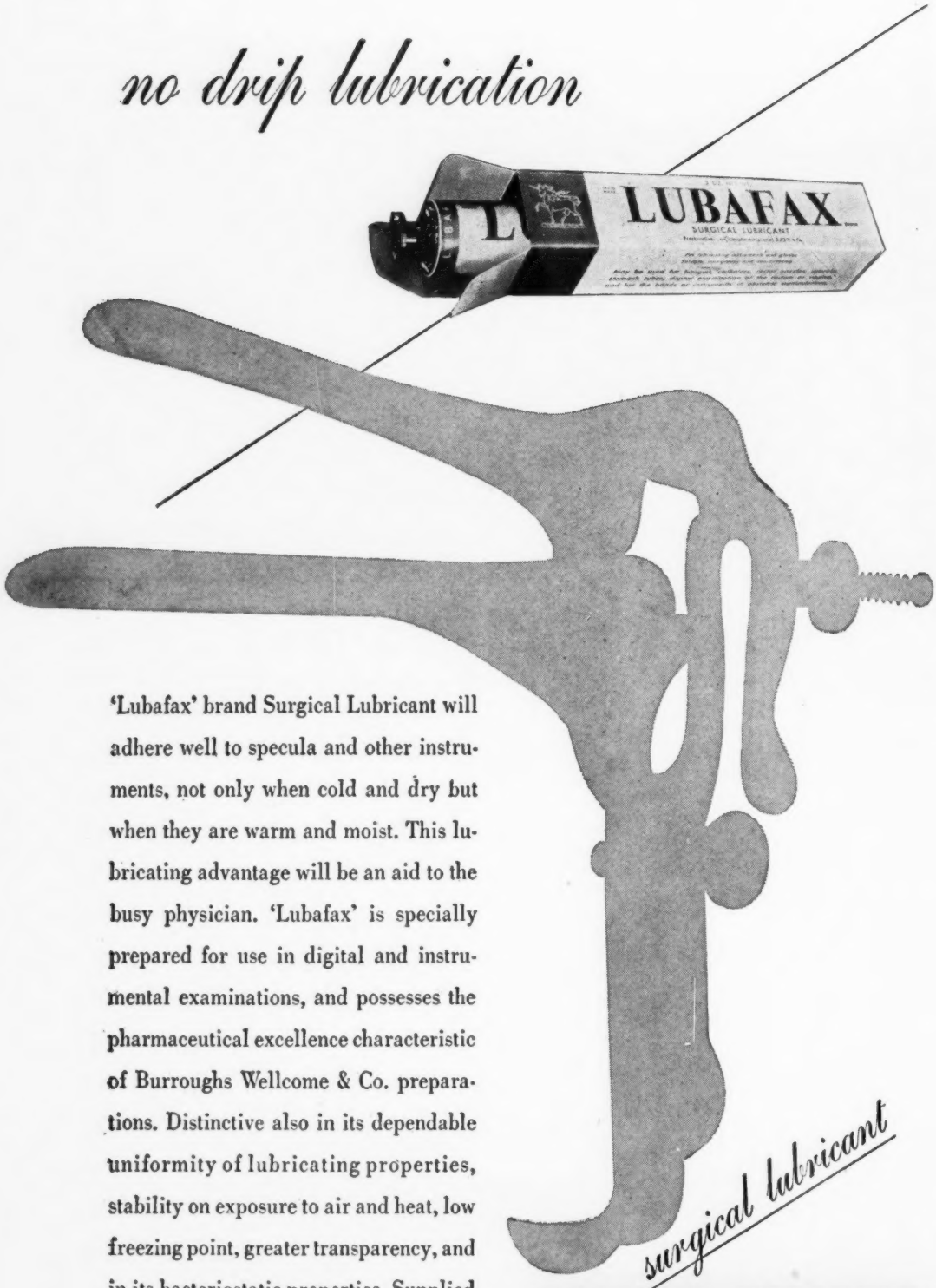

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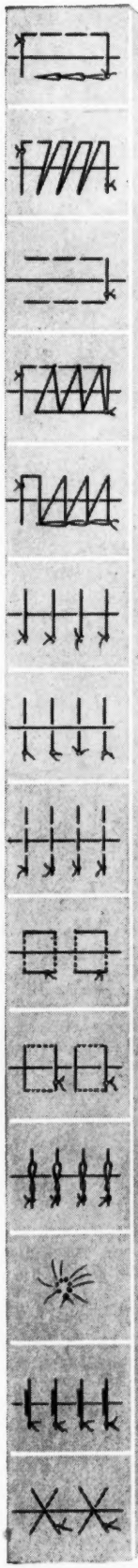

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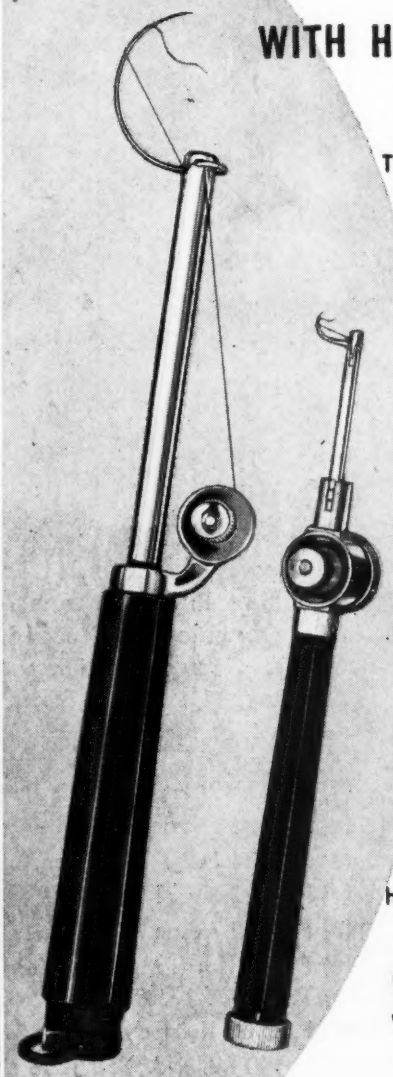

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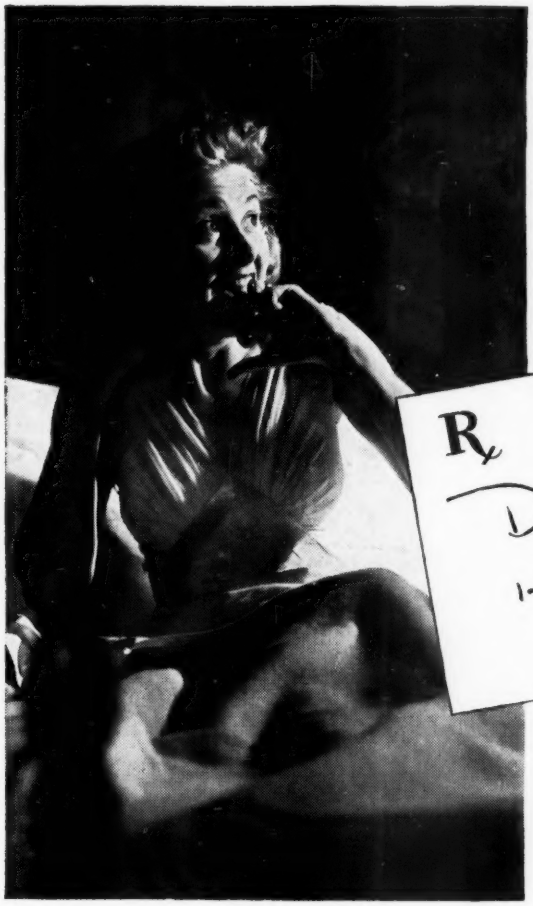

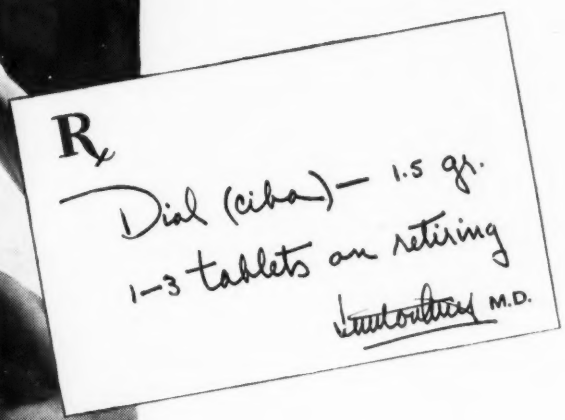

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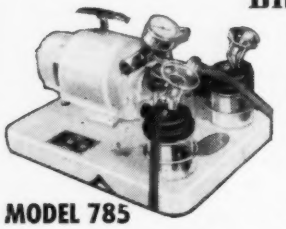

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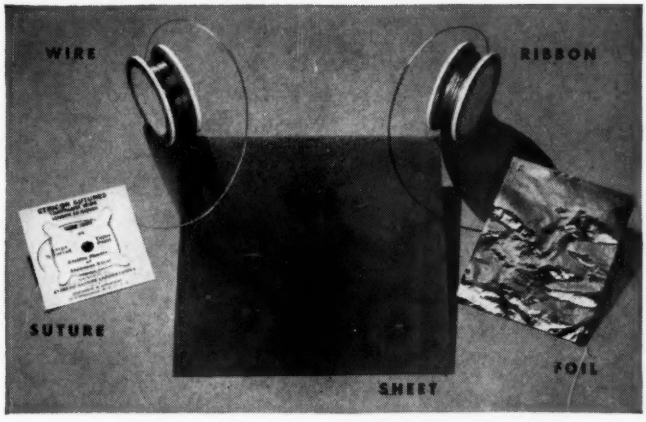

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SURGERY

VOL. 20 JULY, 1946 NO. 1

Original Communications

Society of University Surgeons

TECHNICAL CONSIDERATIONS IN SURGICAL THERAPY FOR COARCTATION OF THE AORTA

ROBERT E. GROSS, M.D., BOSTON, MASS.

(From the Surgical Service of the Children's Hospital and the Department of Surgery of the Harvard Medical School)

IN THE "adult type" of coarctation there is a narrowing or complete obstruction of the aorta at or near the ductus arteriosus or its obliterated remnant. Individuals with this abnormality have a variable prognosis; some survive for a surprisingly long time and have relatively mild symptoms, but most of them have a life span which is far short of the normal expectancy. They may have complaints which arise directly from the arterial obstruction, or they may have a serious disorder from one of its complications. These include (1) aneurysmal dilatation of the aorta, particularly above the constriction; (2) rupture of the aorta; (3) formation of a dissecting aneurysm; (4) superimposed *Streptococcus viridans* infection; (5) development of high blood pressure in the upper part of the body, with all of the attendant dangers of the hypertensive state. In the future it is probable that local bacterial infections can be efficiently combated in many instances by modern methods of chemotherapy. However, the other complications have little promise of relief, and because of this state of affairs there is a real impetus for finding ways in which the coarctation of the aorta might be corrected.

Our observations in the experimental laboratory[6] indicate that it is technically possible to remove a segment of the thoracic arota and to reconstruct the vessel by end-to-end anastomosis. With this background, five human patients have been operated upon in this clinic for coarctation of the aorta with very promising results. Additional evidence that such operations can be successful in man is brought forth by the report of Crafoord and Nylin.[4] Although experience in this field of surgery is still limited, it appears that removal of an

Presented at the annual meeting of the Society of University Surgeons, New York N. Y., Feb. 7-9, 1946.

anomalous aortic segment can be accomplished without too great a risk and that hypertension in the upper part of the body can be relieved. These procedures are new and will possibly undergo modifications as additional information is gained. However, I would like to discuss some of the technical details which have been formulated or have been found to be of value during such operations on human subjects.

Anesthesia.—Anesthesia with ether should be satisfactory, but cyclopropane would seem to be preferable—and was used in all of our cases. It is necessary to have some sort of a closed system to administer the anesthetic so that the intrapulmonary pressure can be controlled at will. However, an intratracheal tube is not essential, and I believe that it is better to omit it. A closed system was maintained in our patients by merely using a tightly fitting face mask. With such arrangements, anesthesia, even though quite prolonged, was completely satisfactory and could not conceivably be improved.

Vein Cannula.—It is now a common practice to prepare for major surgical undertakings by inserting a needle into a vein of an extremity prior to operation to facilitate the administration of fluids and blood during and after the procedure. Certainly, for operations upon the aorta, this precaution will add greatly to the operator's peace of mind because he is assured that blood can be given in an instant if conditions demand it. Bleeding from the aorta or its anastomosis should be minimal or nil, but the great vascularity of the chest wall will sometimes lead to a serious loss of blood while the thorax is being opened and it may be necessary to compensate for this. A sharp needle may not be wholly satisfactory because it can be disturbed at a crucial moment and can penetrate the back wall of the vein, thus being thrown out of commission just when it is needed most. It is better to cut down on a vein, preferably of the ankle, to insert a blunt cannula of moderate size (No. 14 or 15) which can be tied into the vessel, and which can be relied upon to function perfectly for a period of many hours. Attached to this needle should be an infusion apparatus, the tubing of which contains a three-day stopcock, arranged in such a way that blood will pass through it slowly from a suspended bottle, or else a syringe can be attached to its sidearm for pumping blood through the system under pressure if this should be required.

Operative Approach.—Much can be said in favor of an anterior or an anterolateral thoracic approach to the aortic arch and the first part of the descending aorta. With this avenue the thorax can be opened quickly, the division of chest muscles is minimal, and the resulting exposure is wide. The closure of such a wound is relatively easy and the postoperative discomfort to the patient is distinctly less than is the case with a posterior incision. Much of the experimental work on dogs was done through an anterior opening, but it soon became obvious that conditions were not optimum for manipulating and rotating the aorta to expedite suture of its ends. In contrast, a posterior incision will allow clamps to be placed on the aorta in such a way that they can be rotated forward and thus provide room for the operator to sew the back wall of the aorta; subsequently the clamps (and aorta) can be turned backward so that the anterior edges of the vessel can be stitched. This single and important fact

led to the adoption of a posterior approach in all of the more recent animal experiments and in each of the human operations. Without question, the aortic arch and the first part of the descending aorta can be clearly viewed through an anterior chest wound, but in order to work effectively upon this vessel, to free it from its bed with safety, to mobilize it, to remove the narrowed segment, and to suture its free ends, a posterior thoracic approach is much superior.

Opening of the Chest.—The incision must be liberal. It runs along the medial and inferior borders of the left scapula in a downward and outward direction, extending from the level of the second dorsal vertebra superiorly to the midaxillary or anterior-axillary line inferiorly. That portion of the trapezius which presents beneath this cutaneous opening is cut across. The broad belly of the latissimus dorsi muscle is completely transected, at right angles to the direction of its fibers. The rhomboideus major and minor muscles are divided near their attachments to the medial border of the scapula. The scapula can then be displaced upward and outward so that the underlying bony cage of the thorax is brought into view. The fourth rib is removed subperiosteally from its midaxillary zone around to its tubercle. From the third, fifth, and sixth ribs a segment, 3 to 4 cm. long, is cut out from the rib angle well down to the tubercle. The pleural cavity is now entered by incision throughout the bed of the fourth rib. At its medial end this incision is connected with a vertical one running up through the previously exposed bed of the third rib and similarly running downward through the fifth and sixth rib beds and intercostal muscles. When a self-retaining retractor is inserted, an adequate exposure of the interior of the chest and the operative field can be obtained.

Opening of the thorax may entail more difficulty than had been anticipated, because of the extreme vascularity of the various structures. Pathologists have often commented upon the large collateral channels which are associated with aortic obstruction, and clinicians have frequently described the pulsating arteries in the soft tissues of the back. The surgeon must be cognizant of these sizable vessels; indeed, he cannot ignore them. The vascularity of the region is so great that considerable time is consumed in clamping, tying, and suturing bleeding points to obtain proper hemostasis. Blood loss may be great, and it is important to cover this adequately by transfusion so that the patient is kept in a stable condition.

Freeing of the Aorta.—The aorta is exposed by longitudinal incision of its overlying parietal pleura from the mid-thoracic area well up over the aortic arch and over the left subclavian artery. With little difficulty, this covering is peeled posteriorly and anteriorly. It is well to keep the dissection fairly close to the aorta and to leave but little areolar and fatty tissue on the vessel. The narrowed portion of the aorta can be readily seen and palpated. The external diameter at this level may be a poor indication of the size of the lumen, but squeezing the vessel between the thumb and forefinger will give some idea of the dimensions of its internal opening. Sometimes the vessel is deeply notched and a high degree of obstruction is readily discernible. In other instances the external indentation is mild and is seemingly not far from normal; still there can be such a great thickening of the vessel wall at this site that the lumen of the

aorta is no more than 1 or 2 mm. in diameter; indeed, it may be completely blocked. Coarctation occurs at a variable distance from the left subclavian artery. In some subjects it is just below the origin of this artery, whereas in others it may be as much as 2 or 3 cm. beyond it. Obviously, the lower constrictions are more amenable to treatment, but a high position of the coarctation, just beyond the left subclavian artery, does not militate against surgical removal of the narrowed segment, as was shown by our fifth patient.

A considerable section of the aorta, as well as the distal part of the arch, must be raised from its bed to facilitate the subsequent steps. This implies that certain vessels shall be severed to free the aorta from surrounding structures. Just below the coarctation at least two sets of intercostal arteries should be doubly ligated and divided. While these arteries may be enlarged to a diameter of 5 or 6 mm., they are apt to be quite thin and should be handled accordingly. Great caution must be exercised to avoid shearing off an intercostal artery as it leaves the aorta, a region of great anatomic weakness. Such an accident gives rise to bleeding which is very difficult to control, and the seepage of blood through the adventitia greatly obscures the field and hampers the dissection. Such mishaps were at times encountered in dogs; they were completely avoided in the human beings by exceedingly careful techniques. It might be necessary to divide one or two sets of intercostal arteries above the coarctation; the existence of such vessels appears to be a variable finding. (Apparently Crafoord has not divided intercostal arteries, but has temporarily clamped them. I believe it is much better to sever them since this permits mobilization of the aorta and it likewise keeps unnecessary clamps out of the field.)

On the anterior surface of the aorta, one or two bronchial arteries will almost certainly require division, depending upon the level at which these arise from the aorta. These vessels are small and can be cut with impunity.

The ligamentum arteriosum (or ductus arteriosus) must then be cut, and when this is done the operator is immediately conscious of a high degree of mobility which has been gained for the aortic segment. Six or seven centimeters of the aorta can then be drawn up into the field. This freed portion is most easily handled by passing linen tape around it. Any remaining bands of areolar tissue which connect it to its bed are cut away. The dissection is carried well up behind the distal third of the aortic arch and up for several centimeters behind the left subclavian artery.

Structures to Avoid.—Within the mediastinum are two anatomic structures which must be kept in mind and constantly avoided. The first of these is the left vagus nerve and the recurrent laryngeal nerve which arises from it. This branch courses below and around the ligamentum arteriosum and then upward on the posteromedial surface of the aortic arch. These nerves can be easily identified after the parietal pleura is opened; they can be peeled off the aorta and the ligamentum arteriosum in such a way that they are left undisturbed and uninjured.

Likewise, great care must be exercised to leave the thoracic duct undisturbed. This lymphatic channel lies against the vertebral column and should be found between the right and left intercostal arteries just after they leave the

aorta. In some human beings the duct stands out clearly and can be readily identified. In others, it is small or is obscured by overlying fat so that it is difficult to find. Possibly the vessel could be seen more clearly if any appropriate dye were fed before operation or were injected into the lower part of the body so that it appears in the duct. Whether or not the duct is seen, it can be saved from injury by keeping the posterior and medial dissection very close to the aorta itself and not letting the instruments get into the deeper tissues which contain the duct.

Clamps for Aorta.—A pair of clamps must be provided for maintaining hemostasis during the subsequent period when the aorta will be opened. It is also highly desirable to have these clamps in such a form that they can be used to manipulate the aorta. In laboratory work it was found that full-lengths, Kelly clamps, Kocher clamps, etc., would grasp the aorta tightly, but the rigid jaws were apt to traumatize the vessel to a disturbing degree. Bethune clamps gave good hemostasis, but they wrinkled the aorta too much. A wide variety of instruments were tried, but for one reason or another they were all discarded. The best results were obtained by revamping a pair of Moynihan, straight intestinal clamps and using them without rubbers. The jaws were cut off to a length of 5.5 cm.; the tips were fitted with an interlocking peg so that the two jaws could not wiggle sideways from one another when the clamp was closed. With such an instrument, considerable pressure can be exerted on a large vessel, and yet the jaws possess sufficient resiliency so that there is very little crushing effect. The clamp cannot slip sideways because the longitudinal slits in the jaws grasp the adventitia securely. Furthermore, endwise slipping of the clamp is guarded against by cross-marks filed on its inner surfaces. The instrument will accommodate vessels varying in size from the smallest to the largest which might be expected.

Suture Material.—Obviously, the suture material must be of a nonabsorbable type. Silk was employed in all of the experiments with animals and with human beings. An interwoven variety is far superior to a twisted one because it has higher tensile strength, smaller caliber, and no tendency to fray out. Deknatel (00000) is an appropriate form and size. This is carried on an atraumatic needle so that an exceedingly small hole is made when the aorta is pierced. While a slightly curved needle has some advantages, a straight one about 15 mm. long is preferable.

Excision of Aortic Segment.—The two clamps are placed upon the aorta in such a way that a portion 1½ or 2 cm. long can be cut out and discarded. In addition, sufficient room (almost 1 cm.) must be left inside of either clamp to provide a cuff which can be used for anastomosing the remaining vessel ends. When the aorta has been divided, these cuffs immediately shrink; they may become so short that it is very difficult to sew them in an accurate fashion. Hence it is imperative, when affixing the clamps, to make due allowance for shrinkage of the vessel ends which will invariably take place when the aorta is transected.

While the aorta is being severed, one must constantly keep in mind the sizes of the upper and lower orifices which are being produced. These must have ap-

proximately the same dimensions to permit proper anastomosis. In order to accomplish this, it might be necessary to cut the upper or the lower part on a little slant to produce an end of appropriate size.

The segments of aorta which were removed from the five human patients showed extreme degrees of obstruction. Four of the specimens possessed a lumen no more than 2 to 2.5 mm. in diameter, while the fifth had a complete diaphragm and no opening at all.

Method of Aortic Anastomosis.—For aortic anastomoses, Crafoord and Nylin have employed a technique which has been generally used for vascular suture for many years. With this Carrel method of triangulation, the ends of the vessel are brought together by three interrupted stitches placed at equidistant points around the circumference of the vessel, and then each of these limbs sewed with a running stitch. The description would seem to imply that the ends of the aorta can be held together with the three interrupted sutures while the vessel is being repaired. While this may be true, it is well to emphasize that when the aorta is transected, its ends separate from one another in a very distressing way. Hence, any attempt to overcome this great tension by holding the aortic ends together with a few interrupted stitches would seem to be fraught with dangers and pitfalls. Instead, it has been my plan to have a well-instructed first assistant manipulate the two clamps, and to hold them so that they are pushed toward one another, a movement which brings the ends of the aorta together and removes all tension from the suture line while the anastomosis is being performed.

In the laboratory, experiments have been carried out with various methods of aortic suture and it is felt that the usual type of Carrel stitch, whereby the vessel ends are butted together with an over-and-over stitch (including all layers of the wall), will often give a successful anastomosis, but that it cannot be relied upon to accomplish this task uniformly. Without question, the method par excellence is that in which a continuous, mattress type of stitch includes all layers and brings intima to intima, turning the vessel ends outward. This technique was used in all of our cases; the procedure has been described and illustrated in a previous communication.[6] The thread must be drawn up with appropriate tension and must not be relaxed while a subsequent stitch is being taken. It is well to delegate the holding of the thread to a second assistant whose attention is not deflected by any other duty at the moment. The most difficult part of the anastomosis is on the posterior surface of the aorta, hence the stitching should be started here and then continued around on the anterior wall. The first assistant can rotate the clamps to give the best exposure of the posterior or the anterior wall of the aorta as the operator requires. After the anastomosis is completed the lower clamp is removed or temporarily loosened. With this maneuver some blood will flow back into the area under a relatively low pressure and the line of anastomosis can be quickly tested. In one or two points there may be pinhole openings, but these can be closed with a few interrupted stitches. If the original stitching has been properly performed, there is little or no oozing. It is highly important to emphasize that the use of packs, fibrin foam

with thrombin, or other anticoagulants is not needed for buttressing the suture line if the anastomosis has been done accurately. In none of the five human cases was it necessary to employ any such secondary methods for hemostasis.

Prevention of Cardiac Collapse.—From some of our experimental work, and from a disastrous outcome in one case, it is evident that a quick removal of the last aortic clamp may impose a momentary but serious burden on the cardiovascular apparatus. The sudden opening up of an enormous vascular bed in the lower part of the body makes great demands upon the heart. The cause of death in the first patient has been loosely described as "cardiac collapse," since the exact mechanism of failure is not known. Presumably, it was a form of "shock," because blood flowed rapidly into the depleted system in the lower two-thirds of the body, pooled there, and did not return quickly enough to supply the heart with a circulating medium. Having these thoughts in mind, certain measures were taken in the last four patients to prevent cardiac failure at this stage by (1) removing the remaining (upper) aortic clamp gradually over a period of five or six minutes so that the rush of blood into the lower aortic segment would be retarded somewhat; (2) tipping the patient into a mild Trendelenburg position to facilitate the return of blood to the heart, and (3) quickly injecting 150 to 250 c.c. of blood (under pressure) into the ankle vein cannula to augment the circulating fluid. With such precautions, there was very little change in the rate or amplitude of the heartbeat, and the readjustments in the circulation were completed without the slightest apprehension.

Closure of the Chest.—Of primary consideration in the thoracic closure is the avoidance of large vessels in the chest wall; the puncture of which will allow bleeding into the pleural cavity. Such hemorrhage is apt to be particularly troublesome in the vertical part of the T-shaped wound (that part parallel to the spine). Hence, it is well to start the closure here so that the interior of the chest can be viewed from time to time to make certain that blood is not running into it. If this occurs, additional sutures can be appropriately placed to obtain hemostasis. The lateral part of the wound is now closed by approximating the edges of the bed of the fourth rib. If the needle is kept well within this bed, and not allowed to go out into the adjacent intercostal muscles, bleeding is avoided or kept to a minimum. The superficial muscles are suitably repaired.

The lung can be expanded by increasing the pressure in the anesthesia machine, but I am convinced that there is less postoperative disturbance in the lung if it is expanded by sucking out all fluid and air from the pleural cavity. This can be done quickly and effectually by inserting a large catheter into the pleural cavity, aspirating through it, and then withdrawing it just before the skin is closed.

Postoperative Care.—There is little to add regarding the postoperative care of these individuals, except to state that it can be made extremely simple. Oxygen tents are unnecessary if the lung has been adequately expanded at the termination of operation.

In the four surviving patients, the wound healed per primam. Because of the length of the operative procedure, and because of the possible accumulation

of sanguineous fluid within the pleural cavity which would be a good culture medium, it was deemed advisable to prescribe penicillin and sulfadiazine for five or six days after operation. These drugs are probably unnecessary and good results can undoubtedly be obtained without them, yet it appears to be expedient to employ them in the immediate postoperative period.

Posterior chest wounds may give a great deal of pain if rib ends are improperly mobilized and are allowed to rub together during respiratory movements. Conversely, postoperative pain can be kept at a minimum and sedation can be reduced if a segment of rib is always removed so that the ends of bone cannot touch each other during the postoperative period. The ribs will regenerate from the periosteum which is left.

It is not necessary to administer dicoumarin or heparin to prevent local thrombosis. If the aorta is not damaged by instruments, and if a proper anastomosis has been performed, the danger of regional thrombosis is insignificant.

It may be necessary to withdraw fluid from the left pleural cavity during the postoperative period. In two of our patients the chest was aspirated once during the first postoperative week and a considerable amount of thin hemorrhagic fluid was taken away. There was no reason to suspect leakage from the aorta since the anastomosis lines were left completely dry at the time of operation. Such an accumulation of pleural fluid was almost certainly due to oozing from the thoracic wall.

SUMMARY

Coarctation of the aorta is a congenital abnormality which can be corrected by direct surgical attack on the lesion. The narrowed or completely obstructed segment can be excised, and the remaining portions of the aorta can be brought together by an end-to-end anastomosis. Five patients have been thus treated; the first died of cardiac failure during operation, while the other four have made very satisfactory recoveries. Laboratory experimentation which led to development of this technique, plus the experience which has been gained from the human cases, form the bases for the various remarks which are listed here as technical considerations in surgical therapy for coarctation of the aorta.

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ARTERIOVENOUS FISTULAS AND ARTERIAL ANEURYSMS IN MILITARY PERSONNEL

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AS IS well known, arteriovenous fistulas and arterial aneurysms result from trauma, congenital anomalies, and infection, and arterial aneurysms from arterial disease as well. The congenital and traumatic aneurysms and fistulas are generally amenable to operative treatment. On the other hand, surgery is less uniformly applicable in the cure of aneurysms resulting from arterial disease for two reasons: first, the preponderance of these lesions in the aorta which can rarely be ligated without disastrous consequences or successfully repaired and, second, the frequently precarious state of the collateral circulation in limbs in which such aneurysms exist, which is due to the associated obliterative arterial changes. Congenital aneurysms and fistulas are relatively rare, and traumatic aneurysms and fistulas occur commonly only in time of war. Because of these considerations it has not often been possible for any individual or group to treat large numbers of these lesions and, consequently, reports concerning their surgical management generally deal with single cases or small series of cases.

During the recent war the staffs of the three Vascular Centers established by the Surgeon General have studied and cared for large numbers of soldiers with aneurysms and arteriovenous fistulas. We have had opportunity to treat many such patients at the Vascular Center at the Mayo General Hospital and to study others who were operated upon elsewhere. It is believed that a brief general discussion of this experience and of some of the problems encountered may prove worth while. No attempt will be made in this report to present in detail certain specific problems which can be discussed more profitably in separate reports. In addition, for the further sake of brevity, in this communication will be omitted references to the large body of constructive clinical and experimental studies which have been recorded in the literature and which have, throughout the years, rendered the surgical treatment of aneurysms and fistulas progressively safer and more successful.

CLINICAL MATERIAL

This study comprises 364 arteriovenous fistulas and arterial aneurysms which occurred in 351 individuals. There were 245 arteriovenous fistulas and 119 aneurysms. The material consists of three groups: first, 206 arteriovenous fistulas and 82 arterial aneurysms which we treated by operation at the Mayo

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General Hospital;* second, 34 arteriovenous fistulas and 29 arterial aneurysms operated upon in other army medical installations and studied subsequently at the Mayo General Hospital; and third, 5 arteriovenous fistulas and 8 arterial aneurysms which underwent "spontaneous cure" by thrombosis and required no operative treatment. Multiple lesions occurred in 9 patients who had a total of 22 fistulas and aneurysms. One arterial aneurysm resulted from acute medial necrosis, 2 intracranial carotid aneurysms were without known etiology, and 7 arteriovenous fistulas in 5 persons were congenital. One patient with signs of aortic valvular disease had a large mycotic aneurysm of the popliteal artery which almost certainly resulted from subacute bacterial endocarditis with embolism. The remainder were traumatic in origin.

SYMPTOMS, DIAGNOSIS, AND LOCALIZATION

Many of the patients had no symptoms referable to the aneurysm or fistula. Others were aware only of an abnormal pulsation, a pulsating mass, or a bruit or thrill. Those with intracranial aneurysm had headache and ophthalmoplegia, and those with fistula of the carotid artery and the cavernous sinus noted a buzzing noise in the head and a pulsating exophthalmos associated with ocular palsies. When subcutaneous rupture or rapid expansion of an aneurysm occurred there was often intense pain and sometimes loss of nerve function. In a few patients there was fatigue on exercising the limb in which the aneurysm or fistula was situated.

Those patients with cardiac dilatation resulting from an arteriovenous fistula sometimes had no related symptoms, but in a number of them there was dyspnea on exertion, palpitation, or an uncomfortable sense of pounding of the heart, particularly in the recumbent position. Evidence of definite myocardial insufficiency was present, however, in only two instances. One was in a patient who had a traumatic fistula of the external iliac artery and vein and also of the hypogastric vessels. Great dyspnea, orthopnea, and edema had developed shortly after the injury. These symptoms disappeared following resection of the iliac fistula in a hospital overseas. The second fistula was subsequently recognized and its excision brought about further reduction in size of the heart. In the other patient vegetations developed within a femoral arteriovenous fistula which gave rise to a *Streptococcus viridans* septicemia. He had pulmonary infarction and extreme orthopnea. Symptoms subsided rapidly after excision of the fistula.[1]

In general, diagnosis presented no great difficulty. The signs present in arteriovenous fistula have long been recognized and are so precise and constantly present that they render diagnosis relatively easy. In the cases studied, a continuous bruit was invariably present, and a continuous thrill was absent in only a few instances where the fistula was very small. With a single exception there was a definite bradycardic reaction during compression of the fistula, and almost as regular was an elevation in blood pressure during

*This group includes one patient operated upon by one of us (H. B. S.) overseas in the 118 General Hospital and four operated upon at the Percy Jones General Hospital during the brief period when the Vascular Center was located there. For the sake of convenience these five patients will be included with those who were treated at the Mayo General Hospital.

this procedure. Often there was a rise in both diastolic and systolic pressure, the former occurring more uniformly and in greater degree than the latter. Generally the frontal cardiac area was demonstrably increased on roentgenographic examination in instances where there was a large fistula, with the exception of lesions of the carotid vessels in which cardiac enlargement was usually absent.

In cases of arterial aneurysm there was sometimes present a pulsating mass, a systolic bruit, and a systolic thrill. Not infrequently, however, a pulsating mass was not visible or palpable, particularly when the aneurysm was of small size and was covered by large muscles. Nevertheless, an abnormal pulsation was almost invariably present. With rare exception a pronounced systolic bruit was audible, but often the systolic thrill was absent. In two cases of intracranial aneurysm neither bruit nor thrill was present, but the correct diagnosis was suspected because of signs of ophthalmoplegia and was confirmed by arteriogram. Twice a mistake in diagnosis was made. One was in a patient with a very tense nontraumatic popliteal aneurysm without bruit or thrill which, before operation, was considered probably a cyst with transmitted pulsation rather than an arterial aneurysm. The other was in a patient who had an abnormal pulsation in one infraclavicular region associated with a loud systolic bruit and a foreign body visible by roentgenography in the clavicular area. Exploration was carried out in this patient under the impression that the condition was due to an aneurysm, but it was subsequently established that it was dependent upon costoclavicular compression of the subclavian artery.[2]

The correct localization of the aneurysm or fistula was generally easy, and in only a few cases was an error in localization made. The commonest difficulty arose in cases with lesions of the profunda femoral vessels in which the pulsation, bruit, and thrill could be eliminated only by compression of the overlying femoral as well as of the involved profunda vessels. In one instance a fistula between the internal mammary artery and the innominate vein was thought before operation to be a fistula of the innominate or subclavian vessels. In another patient who had a fistula between the transverse cervical artery and the internal jugular vein, exploration was done with a preoperative diagnosis of subclavian arteriovenous fistula. Still another patient with a fistula between the inferior geniculate artery and the popliteal vein was believed to have a popliteal arteriovenous fistula.

ARTERIOGRAMS

Arteriograms were made in a number of instances. The technique employed and the indications for this procedure and its value will be presented in another publication. It is our belief that such studies, although not without hazard, are reasonably safe. No reactions occurred, and good visualization of the lesion was obtained with relatively small amounts of 70 per cent diodrast. Arteriograms were found particularly helpful in cases of intracranial aneurysm without bruit or thrill where confirmation of the diagnosis was advisable before ligation of the carotid artery. They were very useful

in cases in which one could not be certain of the exact localization of the lesion, particularly when tests showed the collateral circulation to be poor and when the lesion might conceivably involve either some very important artery, such as the femoral, or a relatively unimportant one such as the profunda femoris. Arteriograms were likewise of considerable aid in cases in which it appeared that the aneurysm was being "cured" by thrombosis. It was found that arteriograms were unnecessary in the great majority of cases either for correct localization or for proper surgical treatment of the fistula or aneurysm.

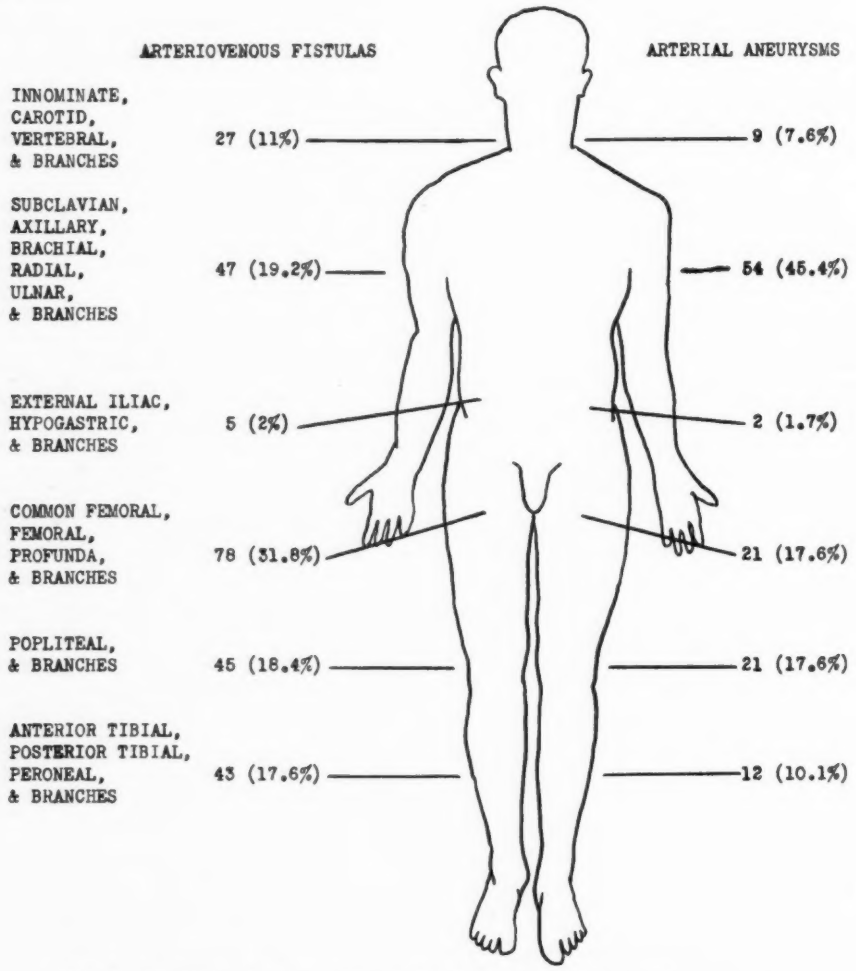

Fig. 1.—Diagram showing general distribution of fistulas and aneurysms.

DISTRIBUTION OF LESIONS

In Fig. 1 the general distribution of the aneurysms and arteriovenous fistulas is shown, and in Table I the lesions are listed according to the affected artery. There were lesions of all the main peripheral arteries with the exception of the common iliac, and of most of their branches. There were no

aneurysms or fistulas of the abdominal aorta, but there were a few patients with involvement of the external iliac, hypogastric, superior gluteal, and obturator vessels. In five instances the aneurysm or fistula was within the anterior mediastinum. There were two intracranial aneurysms and two intracranial fistulas. The majority of the lesions were in the vessels of the limbs.

Important arteries, such as the aorta, the innominate, carotid, vertebral, subclavian, axillary, brachial, iliac, femoral, and popliteal, were affected in 162 of the 245 arteriovenous fistulas (66 per cent) and in 94 of the 119 arterial aneurysms (79 per cent). Less important arteries, such as the radial, ulnar, anterior or posterior tibial, peroneal, obturator, hypogastric, and branches of the main arteries, were involved in the remaining 34 per cent of the arteriovenous fistulas and in 21 per cent of the arterial aneurysms.

TABLE I. DISTRIBUTION OF ANEURYSMS AND ARTERIOVENOUS FISTULAS

	ARTERIOVENOUS FISTULAS, NUMBER OF CASES			ARTERIAL ANEURYSMS, NUMBER OF CASES		
ARTERY INVOLVED	OPERATION AT M. G. H.	OPERATION ELSEWHERE	"SPONTANEOUS CURE"	OPERATION AT M. G. H.	OPERATION ELSEWHERE	"SPONTANEOUS CURE"
Aorta	1					
Innominate				1		
Internal carotid	3			2		
External carotid	3					
Common carotid	6		1	1	1	2
Vertebral	4					
Lingual	1					
Occipital	1					
Cirsoid, nose, ear	2					
Superior temporal	2			1		
Transverse cervical	1	1				
Deep cervical				1		
Internal mammary	1					
Subclavian	6	3	1	5		
Axillary	12			13	2	
Branch axillary	4			2		
Brachial	11	1	1	22	5	1
Radial	1	1		2		
Ulnar	4	2		2		
External iliac		1		1		
Hypogastric	1					
Superior gluteal	2			1		
Obturator	1					
Common femoral	3	2				1
Femoral	47	13	1	6	9	1
Profunda femoris	6			2		
Branch profunda	2	2	1	2		
Popliteal	41	1		14	6	1
Geniculate	4					
Posterior tibial	21	5		1	4	2
Anterior tibial	5	1		2	1	
Peroneal	5	1			1	
Branches in calf	5			1		
Total	206	34	5	82	29	8

It is of interest that the subclavian and popliteal vessels were involved in about the same percentage of cases in the group of arteriovenous fistulas and in the group of arterial aneurysms. On the other hand, the axillary and brachial vessels were much more commonly affected in the group of arterial aneurysms, whereas the femoral vessels were involved with greater frequency

in the group of arteriovenous fistulas (Table II). The incidence of arterial aneurysms of the femoral vessels was only one-half that of the arteriovenous fistulas, but was two and one-half times as great in the case of the axillary and four times as great in the case of the brachial vessels. It is entirely likely that the common occurrence of arteriovenous fistulas in the femoral vessels may be linked with the relative fixation of the artery and vein to one another and to the surrounding tissues. Conversely, the greater frequency of arterial aneurysms in the axillary and brachial arteries may be dependent upon the relative mobility and lack of fixation of the distal portion of the axillary and brachial vessels.

TABLE II. COMPARISON OF INCIDENCE OF ARTERIAL ANEURYSMS AND ARTERIOVENOUS FISTULAS IN THE MAIN PERIPHERAL ARTERIES

ARTERY INVOLVED	ARTERIOVENOUS FISTULAS		ARTERIAL ANEURYSM	
	NUMBER	PER CENT	NUMBER	PER CENT
Subclavian	10	4.1	5	4.2
Axillary	12	4.9	15	12.6
Brachial	13	5.3	28	23.5
Common femoral and femoral	66	26.9	17	14.3
Popliteal	42	17.1	21	17.6

In nine patients there were multiple aneurysms and fistulas. One patient had a congenital lesion with three distinct fistulas involving the anterior and posterior tibial and the peroneal vessels. The other aneurysms and fistulas were traumatic in origin. One patient had four arteriovenous fistulas,[3] one had two arteriovenous and one arterial aneurysm, two had one arterial aneurysm and one arteriovenous fistula, and the remaining four had two arteriovenous fistulas each. These multiple lesions generally occurred as the result of multiple wounds by shell fragments or land mines. In one soldier, however, the same fragment of metal produced a fistula both of the external iliac and of the nearby hypogastric vessels. In another, arteriovenous fistulas of the vertebral and of the brachial vessels were caused by injuries received on two separate occasions.

ASSOCIATED INJURIES AND COMPLICATIONS

A number of patients had sustained fractures in limbs in which an aneurysm or fistula occurred. In one, the shattered fragments of the fibula lay within the aneurysmal sac. In a few, amputation had been necessary of an extremity in which an aneurysm or fistula was present. There had been extensive loss of muscles in a number of persons either from ischemia, infection, or direct trauma. A few had superficial gangrene of digits or ulceration of skin. Not infrequently patients with an aneurysm or fistula had soft tissue or bony injuries of other extremities, or thoracic or abdominal injuries. Several had organic valvular heart disease. One has been previously mentioned who had a mycotic aneurysm resulting from an infected embolus. Still another patient has been referred to in whom vegetations which gave rise to *Str. viridans* septicemia developed within an arteriovenous fistula.

TABLE III. PERIPHERAL NERVE LESIONS ASSOCIATED WITH FISTULAS AND ANEURYSMS

ARTERY INVOLVED	ARTERIOVENOUS FISTULAS						ARTERIAL ANEURYSMS					
	NERVE LESION REQUIRING OPERATION		NERVE LESION NOT REQUIRING OPERATION		NO NERVE LESION		NERVE LESION REQUIRING OPERATION		NERVE LESION NOT REQUIRING OPERATION		NO NERVE LESION	
	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT	NUMBER	PER CENT
Brachial	8	61.5	1	7.7	4	30.8	24	85.7	1	3.6	3	10.7
Axillary	9	75.0	0		3	25.0	11	73.3	1	6.7	3	20.0
Subclavian	0		4	40.0	6	60.0	3	60.0	1	20.0	1	20.0
Popliteal	10	23.8	3	7.1	29	69.0	2	9.5	6	28.6	13	61.9
Femoral	5	8.2	16	26.2	40	65.6	1	6.2	3	18.8	12	75.0
Others	10	8.6	17	14.5	90	76.9	7	13.0	13	24.0	34	63.0
Total	42	17.1	41	16.7	162	66.1	48	40.3	25	21.0	46	38.7

By far the commonest complication was an associated peripheral nerve injury. In Table III data concerning these associated nerve palsies are summarized. Eighty-two of the 245 arteriovenous fistulas (33.8 per cent) were complicated by some nerve injury. In about one-half of these, the nerve injury was such as to require operative treatment, either neurolysis or neurorrhaphy. Seventy-three of the 119 patients with arterial aneurysm (61.3 per cent) similarly had associated nerve palsies. In approximately two-thirds of these seventy-three patients, neurolysis or neurorrhaphy was necessary. In the majority of these the associated nerve damage appeared to be the direct result of the initial trauma. In some, however, nerve dysfunction seemed to be partially or wholly the result of pressure by the aneurysm. The patients listed as requiring no surgical treatment had predominantly injuries to sensory nerves, such as the saphenous, which caused no distress or disability. Others had more serious nerve palsies but spontaneous recovery of function took place. A few had injuries of the vagus, the phrenic, or the cervical sympathetic nerves where it was felt that a successful repair could not be achieved or where the resultant paralysis was considered of little importance.

It will be noted in Table III that a very high percentage of the aneurysms or fistulas of the brachial and axillary vessels and, to only a slightly less extent, of the subclavian vessels were complicated by accompanying nerve palsies. Aneurysms and fistulas of the femoral, popliteal, and other vessels less commonly had associated nerve lesions. The high incidence of nerve injuries associated with vascular lesions of the large vessels of the upper extremity appears to be dependent upon the relatively great mass of the nerve trunks and their intimate relationship to the great vessels.

TESTS FOR ADEQUACY OF COLLATERAL CIRCULATION

Elsewhere[4] we have discussed in detail our experience with the various tests for adequacy of collateral circulation in the limbs. We found that the most reliable and practical test which could be carried out before operation was the Matas reactive hyperemia test. Though it was of great aid and general reliability it was found not to be infallible. The chief difficulties arose from the occasional impossibility of compressing accurately the affected artery

at the precise site of the fistula or aneurysm without concomitant occlusion of neighboring vessels. Our experience indicated that if, during the procedure, an excellent and complete flush occurred promptly, without further improvement upon release of the compressed artery, one could operate and ligate the involved artery if necessary with minimal risk of any ischemic difficulty. If, on the other hand, the test seemed indicative of poor or questionably adequate collateral circulation, every effort was made to bring about improvement in the collateral circulation before operation. Another test which, though somewhat difficult to perform, was found to be a useful confirmatory preoperative test was the observation of the extremity for evidence of continued good circulation during prolonged compression of the affected segment of artery. The absence of pulses distal to an aneurysm or fistula in a limb which had maintained good circulation also proved indicative of adequate collateral circulation.

In our experience, the most useful sign which could be elicited at the time of operation was the maintenance of good color and warmth of the hand or foot during a prolonged period of accurate occlusion of the involved segment of the artery with a rubber-shod clamp. If an aneurysm or fistula is explored in a limb in which there is even the slightest evidence to suggest that the collateral circulation may be inadequate, it is imperative that the hand or foot be left undraped during the procedure, that the lesion be approached with great caution, and that extirpation be deferred in case this test is not satisfactory unless it is perfectly apparent that a cure can be brought about with maintenance of the continuity of the affected artery. The presence of good retrograde pulsation in the involved artery also proved a reliable indication of efficient collateral circulation.

With regard to lesions of vessels supplying the brain we have felt it advisable to defer operation until the patient could withstand compression of the involved artery for thirty minutes without subjective or objective symptoms. In addition, we have used electroencephalographic studies performed at rest and during compression of the affected artery in an effort to obtain further data concerning the efficiency of collateral circulation. These studies will be reported subsequently. It may be said that they seemed to shed little or no light upon the problem that could not be obtained by careful observation of the patient during occlusion of the artery.

It must be pointed out that all methods of testing the collateral circulation to the brain or limb are based upon the assumption that no collateral vessel will be unnecessarily sacrificed during the operation, and that no postoperative thrombosis will occur.

METHODS OF INCREASING THE EFFICIENCY OF THE COLLATERAL CIRCULATION

There can be no doubt that one of the most important factors in the development of adequate collateral circulation in cases of arteriovenous fistula is the duration of the lesion. There is less convincing evidence that the same may be true in cases of arterial aneurysm. In general, it may be said that the older the arteriovenous fistula, the better the collateral circulation, and vice

versa. It must be pointed out, however, that numerous exceptions to this observation were found. The collateral circulation was sometimes excellent in cases of only brief duration and inadequate in others of long duration. For example, the inadequacy of the collateral circulation in a limb in which there was a femoral arteriovenous fistula of eleven months' duration was established not only by numerous preoperative tests but by demonstration of extreme pallor and coldness of the foot during temporary occlusion of the isolated artery at the time of operation. Fortunately, in this case, the fistula could be cured with preservation of the continuity of the artery.

As a general rule there is nothing which makes early operation imperative, and in most of the patients included in this study operation was not performed until the lesion was of four months' duration or longer. The economic factor incident to delay in operation and prolonged hospitalization cannot be considered a contraindication to delay, since one cannot subject a patient to added danger of some ischemic disaster upon such grounds. There are, however, exceptions which render delay in operation either hazardous or inadvisable. External rupture of an aneurysm or fistula makes operation imperative, for even momentary delay may endanger the patient's life. Subcutaneous rupture may force early operation because of the associated intense pain, the onset of pressure paralysis, or ischemic difficulties. Similarly, infection in or about an aneurysm or fistula may make it necessary to operate at once. Severe myocardial insufficiency due to a fistula may make early operation necessary. This condition influenced the selection of the time of operation in two patients. The rare complication of infected vegetations within a fistula and septicemia similarly may make delay impossible. By far the commonest factor in rendering prolonged deferring of operation unwise is the presence of associated severe nerve paralysis. There can be no doubt that the earlier such peripheral nerve injuries are treated, the better is the chance for good recovery of function.

Among the several methods available for increasing the collateral circulation are partial proximal ligation of the artery, repeated intermittent digital or mechanical occlusion of the artery, and sympathetic interruption. Partial proximal ligation is applicable only in cases of arterial aneurysm and not in arteriovenous fistulas. This method was used only once in the present series of cases, in the treatment of an innominate aneurysm. In this particular instance definite beneficial results of the procedure were not evident, although its general worth is well established.

Repeated occlusion of the artery is a very useful procedure. Often during the course of such treatment improvement in the efficiency of collateral circulation is so slow, however, that one cannot be certain that the method is actually accomplishing definite results. On the other hand, in other instances one can be quite certain that the compression is hastening the development of adequate collateral circulation, either by rapid progress in the patient's ability to withstand, without the appearance of symptoms, the occlusion of an artery supplying the brain, or by the steady rapid improvement in the collateral circulation of a limb as judged by the reactive hyperemia and other tests.

The third method, sympathectomy, we have utilized extensively. The results of sympathectomy performed in an effort to render the collateral circulation more efficient will be presented in detail in another publication; hence, these experiences will be discussed only briefly here. Seventy-seven sympathectomies were carried out before or at the time of operation. Thirty-six lumbar and twelve dorsal sympathectomies were done in patients with arteriovenous fistula, and seventeen lumbar and twelve dorsal sympathectomies in those with arterial aneurysm. The great majority of the lumbar sympathectomies were done for femoral and popliteal lesions, whereas most of the dorsal operations were carried out for lesions of the axillary vessels. The principal indications for this procedure were as follows: evidence of poor collateral circulation in lesions of adequate duration, definitely impaired circulation in limbs in which paralysis of nerves was present, persistent intense vasospasm, the presence of ischemic lesions in the affected extremity, lesions of important arteries which could not be compressed, making it impossible to test the collateral circulation, and associated causalgia.

The results of the procedure were generally good. Almost invariably tests for efficiency of collateral circulation showed improvement following operation. In many patients the formerly poor collateral circulation appeared to be perfectly adequate either immediately after sympathectomy or during the first few weeks after this operation was performed. In some instances, however, the collateral circulation, although improved, did not appear to be satisfactory. Eventually all of these patients were cured by operative treatment except two who underwent a "spontaneous cure." In those cases where there was evidence of obviously impaired circulation or of intense vasospasm before the performance of sympathectomy, definite improvement in the circulatory status of the limb was noted following this procedure. In general, it was believed that this study confirmed the usefulness of sympathetic interruption in rendering the collateral circulation more efficient. It demonstrated, however, that the procedure has limitations and is by no means infallible. Indeed, the only limb in which gangrene developed immediately after excision of a fistula or aneurysm had been sympathectomized, and similarly the only instance in which ischemic paralysis followed operative cure of an aneurysm at the Mayo General Hospital, was one in which sympathectomy was performed at the conclusion of the operation.

TREATMENT

It is not our purpose to present here in detail the operative approach to lesions of the various vessels or precise descriptions of operative techniques which we have found useful. Certain of these problems have been presented elsewhere[5, 6] or will be discussed later in other reports. We desire, however, to mention briefly some broad principles of surgical management which have proved to be important.

The following objectives should be sought in the operative treatment of aneurysms and fistulas: preservation of life, cure of the lesion, preservation of neighboring structures without injury, maintenance of adequate circula-

tion, and avoidance of disabling scars and contractures. It is therefore important that operative exposure be ample, that one have ready access if possible to the involved and adjacent vessels both proximal and distal to the lesion and to their branches, that hemostasis and asepsis be carefully maintained, and that supportive measures such as the administration of plasma and blood be utilized when advisable. As has been mentioned previously, one should be reasonably certain from preoperative tests of the adequacy of the collateral circulation, and if this fact cannot be established beyond reasonable doubt before operation it should be demonstrated by other tests and observations at the time of operation before any direct attack upon the lesion itself which might entail ligation of the affected artery.

In approaching aneurysms and fistulas it is of the utmost importance that the skin incision be so placed that it permits easy and complete exposure of the involved vessels, and that it be such that it can be lengthened if necessary to make accessible the vessels distal and proximal to the site of the suspected lesion. Furthermore, it is desirable that the incision be one which will yield a good plastic result and will render minimal the hazard of scarring, contracture, and keloid formation, complications which result far too frequently from incisions which follow the course of the vessels longitudinally across the axilla, the antecubital space, and the popliteal fossa, and which cross the normal skin creases of the neck and groin. In this series of cases it was found feasible to utilize skin incisions which were sound from a plastic viewpoint without sacrificing facility or rapidity of adequate exposure of the vessels.[5]

It is our belief, in general, that operations should be done without the use of a tourniquet. We have reserved the tourniquet for large arterial aneurysms or arteriovenous fistulas associated with large saccular aneurysms in which the isolation of the proximal and distal vessels would otherwise have been difficult and would have entailed much needless and perhaps damaging dissection. There are several advantages of operating without a tourniquet. Chief among these is the fact that the localization of the lesion is facilitated by the presence of the pulsation, bruit, and thrill, especially in the case of arteriovenous fistulas, and the fact that observation of the color and warmth of the limb during precise temporary occlusion of the involved artery is such a valuable aid in confirming the efficiency of the collateral circulation.

Arterial aneurysms were treated at the Mayo General Hospital by four methods; excision, intrasaccular ligation of the artery, intrasaccular ligation of the artery followed by excision of the sac, and, in a few instances, proximal ligation of the affected artery. Excision following isolation and control of the proximal and distal artery was utilized chiefly in those instances where the sac was small and where neighboring nerves and vessels could readily be dissected free and preserved from injury. Intrasaccular approach to the artery was employed primarily for large aneurysms not associated with peripheral nerve lesions. In certain instances the artery was dissected out and temporarily occluded above and below the sac; in others the operation was done under a tourniquet. The sac was incised and the openings of the artery were identified. Instead of the usual intrasaccular transfixion of the artery

proximal and distal to the openings, it was our policy to excise a small portion of the sac wall immediately overlying these vessels, to dissect them out individually, and to occlude them with transfixing ligatures. This precaution was taken because we felt it made more certain accurate ligation of the vessels without hazard of injury to neighboring structures such as nerves. We made no effort to obliterate the sac itself by suture; indeed, this was generally impossible because of the huge size of the sac and often because of the poorly developed character of its wall. If any portion of the sac wall could be readily excised, this was done.

Intrasaccular ligation of the vessels followed by complete or subtotal excision of the sac was utilized chiefly in those instances where the aneurysm was closely adherent to nerves which could not readily be freed from it beforehand. The majority of these cases involved the subclavian, axillary, or proximal brachial artery. First the artery was isolated proximally and distally and was temporarily occluded with rubber-shod clamps. The sac was then opened and any laminated thrombus was evacuated. All of the adjacent nerves and trunks were isolated and identified. Ordinarily such operations were done as a combined procedure with members of the neurosurgical section. Only after all the nerves had been freed and identified was the sac excised. Our experience emphasized the importance of such precautions. In a number of cases nerves as large as the trunks of the brachial plexus were so intimately incorporated in the sac wall and so distorted in configuration and color that they appeared not as nervous tissue but as a portion of the sac wall itself. Excision of the sac was generally necessary in order to effect proper surgical correction of associated nerve injuries. Proximal ligation of the affected artery was reserved for the few instances of intracranial carotid aneurysms. Where it was deemed feasible the continuity of the artery was preserved by end-to-end suture, vein graft, or lateral suture, regardless of the method of ablation of the aneurysm itself. In the majority of cases, and in all in which there was any question as to the excellence of the collateral circulation, the concomitant vein was divided and ligated.

The operative technique which was almost invariably used in the cure of arteriovenous fistulas was excision with quadruple ligation of the affected artery and vein together with ligation of branches which communicated with the fistula. In four instances, however, proximal ligation of the artery and vein was carried out—in two cases of fistula of the carotid artery and cavernous sinus, in one case of a high internal carotid-jugular fistula, and in one case of a profunda femoral fistula in which the actual site of the fistula could not be established at the time of operation. In every operation upon an arteriovenous fistula or arterial aneurysm great care was taken to preserve every collateral vessel which was not directly involved in the lesion itself. Each fistula was approached and carefully dissected out with the view of establishing first the feasibility or impracticability of some type of procedure which would make possible the preservation of continuity of the involved artery. When it was possible, the artery was kept intact or was restored by ligation

and transfixion of the fistula, lateral arteriorrhaphy, end-to-end suture, or vein graft.

When it was advisable the fistula was dissected out and was occluded by transfixing ligatures at the point where it joined the wall of the artery. This procedure was employed in eleven patients. In all save one the vein was divided above and below the fistula, and a cuff of vein plicated by transfixing sutures was used to reinforce the ligated fistulous tract. In six cases of aneurysm or fistula, lateral suture was accomplished. Interrupted everting mattress sutures were used and the opening in the artery was closed along the long axis of the rent. In cases of arteriovenous fistula the opening was exposed by section of the attached vein. In ten cases end-to-end suture of the artery was carried out by use of interrupted everting mattress sutures. This type of repair was particularly applicable in lesions of the brachial or distal axillary vessels where the artery could be readily mobilized and length could be gained by suitable posturing of the extremity. In six cases vein grafts were used. These were sutured in place similarly with interrupted everting mattress sutures. In most instances other than those of ligation of a fistula, anticoagulants were used.

Altogether such reparative procedures were accomplished in only thirty-three instances. Several factors made it difficult to restore the continuity of blood flow through the affected artery, particularly since the great majority in our series were traumatic lesions consequent to shell fragments, land mines, or bullets. In these cases the extent of damage to the arterial wall was very extensive in contrast to the limited injury which is the rule when such lesions result from stab wounds, for example. There was frequently gross and much more often microscopic evidence of injury to the arterial wall not only at the site of the aneurysm or fistula but for some distance proximally and distally. Furthermore, most of the arteriovenous fistulas were not simple fistulas but were complicated by one or more false saccular aneurysms as well. Consequently, it was often necessary to excise a portion of the artery, thus eliminating as a possible means of repair the simpler methods such as ligation of fistula or lateral suture. In such cases, end-to-end suture or vein graft was frequently impossible because of the presence of some important collateral artery which emerged so close to the severed end of the artery that it would of necessity have to be sacrificed if repair were attempted. It was our belief that it was unwise to destroy any collateral vessels.

A review of our cases demonstrates that reparative procedures were possible in a larger number of patients than were actually so treated. It is ordinarily unnecessary to attempt any type of restoration of blood flow of the smaller arteries, such as the radial, ulnar, anterior and posterior tibial, peroneal, and the small branches of the larger arteries. If we include only the larger arteries which form the main channels of blood flow into a part, we find that the continuity of the vessel was restored in only 4 of the first 150 such cases (2.7 per cent), whereas this was accomplished in 29 of the last 55 such cases (52.7 per cent). This difference is due, we believe, to the fact that in the first group of patients exploration was carried out with the idea of

attempting arterial repair provided it appeared that normal arterial structures could be utilized and the procedure could be performed without undue difficulty, while in the second group patients were operated upon with the determination to carry out a repair in every instance in which this could possibly be accomplished short of leaving in situ obviously badly damaged portions of arterial wall and of sacrificing collateral arteries.

Those patients described in this review who were operated upon in other hospitals were generally treated by excision or aneurysmorrhaphy in the case of arterial aneurysms, and by excision with quadruple ligation in the case of arteriovenous fistulas.

RESULTS OF TREATMENT

In general, the results of operative treatment were good. Cure of the aneurysm or fistula was achieved in all instances save one. This was a patient with clinical and x-ray evidence of an arteriovenous and a saccular aneurysm in the anterior superior mediastinum. Upon exploration a large aneurysm was found which appeared to involve not only the right innominate and the left subclavian vessels but the arch of the aorta and the superior vena cava as well. The chance of surgical cure appeared technically impossible. Several patients who had undergone surgical exploration and attempt at treatment in other hospitals were subsequently cured at the Mayo General Hospital. Among the 288 aneurysms and fistulas operated upon at the Mayo General Hospital, multiple operations were necessary in six instances. Two of these were cases of vertebral arteriovenous fistula, in one of which the lesion could not be identified at the first operation, and in the second of which a proximal ligation which failed to effect a cure was first attempted. One was an innominate arterial aneurysm in which partial proximal ligation was done at the initial operation because of inadequate collateral circulation. Another was a small aneurysm in the calf which escaped localization during the first exploration. Still another was a femoral arteriovenous fistula in which operative attack was deferred initially because of poor collateral circulation. The last was an arteriovenous fistula of the brachial vessels in which a simple double ligation of the fistula was followed by recurrence of signs of arteriovenous communication. In all instances a cure was effected at the second operation.

The great majority of the patients showed no evidence of circulatory insufficiency after operation as observed at rest and with moderate exercise about the wards. The limbs were well colored, warm, and without diminution in motor power or sensation. On such casual examination the circulation appeared entirely adequate. The activity and the environmental conditions in the hospital are, however, often far different from those which patients will encounter after return to duty or to civilian life. It is consequently necessary to inquire into the ability of such limbs to withstand more strenuous exercise and extremes of environmental change. Upon such testing it was found that a number of patients had complaints which had hitherto been undetected. A certain number of those whose treatment had necessitated ligation of the affected artery had a definite sensitivity to cold. In some, this was so moderate

as to require no further treatment. In others, an annoying sensitivity to cold offered no real problem since the individuals lived in warm climates where they would rarely be subjected to cold temperatures. In those, however, who had such cold sensitivity and lived in cold sections of the country the problem was real and necessitated attempts at correction of the difficulty. When small arteries, such as the radial, ulnar, anterior or posterior tibial, peroneal, and other small branches, had been ligated there was rarely any significant diminution in tolerance of exercise. Furthermore, when the subclavian, axillary, or brachial artery had been ligated there was frequently no subjective complaint on moderate exercise, although ergometric studies and more strenuous exercise generally demonstrated some weakness and fatigability. When the main arteries to the lower extremity had been divided there was, as a general rule, a noticeable fatigability on exercise. Such patients could walk for a given distance but would then have to stop and rest for a moment because of a sense of fatigue or tightness in the calf, following which they could again walk for the same distance before return of the same symptoms. In contrast, most of those patients in whom the continuity of the artery had been maintained noted no significant decrease in the ability to exercise the limb.

Sympathectomy was performed at the Mayo General Hospital in thirty-four instances in order to alleviate certain difficulties which followed operative cure of an aneurysm or fistula. The patients so treated included some who had been treated in hospitals overseas and others who had been treated at the Mayo General Hospital. The chief indications for this procedure were cold sensitivity, obviously impaired circulation in the presence of associated nerve paralysis, and, in a few instances, persistent edema or evidence of continued sympathetic overactivity. As has been mentioned previously, the value of sympathectomy in the treatment of aneurysms and fistulas will be presented fully in another paper. It may be stated here that the results were in general good, although complete alleviation of symptoms did not follow in every instance.

The results of operative repair of arteries were generally excellent. It must be pointed out, however, that of the thirty-three cases in which some type of reparative procedure was accomplished, the success of some appeared very questionable at the time of operation because of extensive damage to the wall of the artery. Repair was attempted in some cases of this sort in order to shed some light upon the limitations as well as the applicability of the procedures. There were six failures among the thirty-three repairs. One of these was the ill-advised simple ligation of a fistula, already mentioned, one was a suture carried out in the presence of gross infection, one was a vein graft in the repair of a brachial artery of unusually small caliber, and three were instances in which the damage to the arterial wall was so extensive that the outcome was obviously questionable. In all instances in which relatively good arterial structures were sutured in the absence of gross infection and in which the caliber of the artery was 3 mm. or greater, the outcome of the procedure was excellent.

So convinced are we that a careful analysis of the complications and difficulties encountered in the treatment of aneurysms and fistulas would be informative that it is planned to devote a separate report solely to a discussion of these problems. It should be mentioned, however, that among those patients operated upon in other hospitals there were a few complications such as ischemic nerve paralysis and operative injury to nerves. These were probably in large part due to the fact that many of them were operations carried out shortly after injury, often of necessity, and frequently before adequate collateral circulation had been demonstrated. There was consequently an additional risk of circulatory difficulty. In early operations there may also be added difficulty in isolating and protecting adjacent nerves. Perhaps the multiplicity of operators may have been a factor also. Among the 288 patients treated at the Mayo General Hospital there were unfortunately six major complications. There were two deaths. One was of a patient with a large aneurysm of the neck arising from the deep cervical artery, who went into profound shock from which he recovered but not before ischemic damage to the brain had occurred which led to his death the following day. Although there was considerable loss of blood it was difficult to account for the severity of the shock on this basis alone, and certain features remain obscure. The other was a patient with a large mediastinal and cervical aneurysm of the subclavian artery treated successfully by proximal and distal ligation of the subclavian artery and ligation of the vertebral artery which emerged from the aneurysm. Death occurred the following day from ipsilateral necrosis of the cerebellum without demonstrable thrombosis of the vertebral artery or the circle of Willis, and without demonstrable embolism. In one patient hemoplegia developed from propagated thrombosis after ligation of the internal carotid artery for the cure of an intracranial aneurysm. Although considerable recovery took place there remained some residual difficulty with fine movements of the hand. Another patient had a transient ischemic nerve paralysis following treatment of a popliteal aneurysm. There was one case of gangrene of the distal third of the foot after excision of a popliteal arteriovenous fistula. In still another patient who had maintained good circulation after resection of a femoral arteriovenous fistula, extensive thrombosis of collateral arterial channels associated with deep venous thrombosis developed on the sixth postoperative day. This led to gangrene of the foot.

SUMMARY

A series of 364 arteriovenous fistulas and arterial aneurysms occurring in 351 soldiers has been reviewed. This included 245 fistulas and 119 arterial aneurysms. The lesions were widely distributed through the body and included involvement of most of the large and small arteries supplying the extremities and the brain. They were largely traumatic in origin. Diagnosis and localization presented no great difficulty. The problem of treatment was often complicated by the presence of associated injuries, particularly of the peripheral nerves. Various tests for efficiency of collateral circulation proved extremely useful but were not infallible. Although the time of operation could

ordinarily be delayed indefinitely in order to permit development of more adequate collateral circulation, certain complications often made earlier operation advisable. Among the various methods of attempting to increase the adequacy of the collateral circulation, sympathectomy was found to be a very useful although not completely reliable aid. The commonly employed techniques of dealing with aneurysms and fistulas were utilized. The special applicability of these methods has been discussed. The problem of restoration of continuity of the affected artery has been presented. The results of treatment were in general good, although two deaths and a number of complications occurred.

Chief among those problems which appear to deserve further intensive study are means of testing more accurately the adequacy of the collateral circulation, methods of increasing the efficacy of the collateral circulation, and the general problem of maintaining the continuity of the involved artery.

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CERTAIN ASPECTS OF BATTLE WOUNDS OF THE THORACIC CAVITY

With Special Reference to a Method of Facilitating Re-expansion of the Lung Following Late Decortication

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AT THE beginning of World War II most thoracic surgeons anticipated that the care of battle wounds of the thoracic cavity would be far superior to that provided in any previous war. I for one anticipated that partial pulmonary resection or the repair of lacerations in pulmonary tissue would be a commonplace procedure. However, experience has shown that the lung has a remarkable ability to recover from penetrating or lacerating wounds so that resection of pulmonary tissue or the suture of lacerations in the lung was seldom found to be necessary. The real therapeutic advances were made in another direction.

During the course of the war it became increasingly apparent that the fundamental objective in the treatment of battle wounds of the thoracic cavity should be complete re-expansion of the lung as early as possible.

Hemopneumothorax.—Before the war there were many who believed that the patient with a simple hemothorax or hemopneumothorax should be treated conservatively and that thoracentesis should be resorted to only in the event of considerable dyspnea. There were others who believed that if the blood were removed by thoracentesis, it should be replaced by air in order to prevent too rapid re-expansion of the lung.

I believe it can be said that as the result of the experience gained in this war, the opinion is now almost universal that better results are obtained by early thoracentesis so as to bring about more rapid re-expansion of the lung. In the campaign of North Burma we were in the favorable position of receiving the wounded early and keeping them until they were well. Early in the campaign I deliberately set out to treat some patients with massive hemothoraces by early thoracentesis and some with no thoracentesis. The conservative treatment was soon abandoned. While it is true that even large hemothoraces were often absorbed, it was observed that the patients took longer to recover and that they were often left with marked residual changes. There was x-ray evidence of considerable thickening of the pleura and physical examination very often disclosed marked fixation of the involved hemithorax.

The primary objection to early thoracentesis in the treatment of hemothorax has been the fear that early re-expansion of the lung might cause a recurrence of the bleeding. This has certainly not proved to be the case. In a series of more than 350 wounds of the thoracic cavity I was never aware that re-expansion of the lung precipitated fresh bleeding. Re-expansion of the lung was usually not attempted until forty-eight to seventy-two hours after injury unless the patient was dyspneic. Seldom was more than 750 to 1,000 c.c. of blood removed

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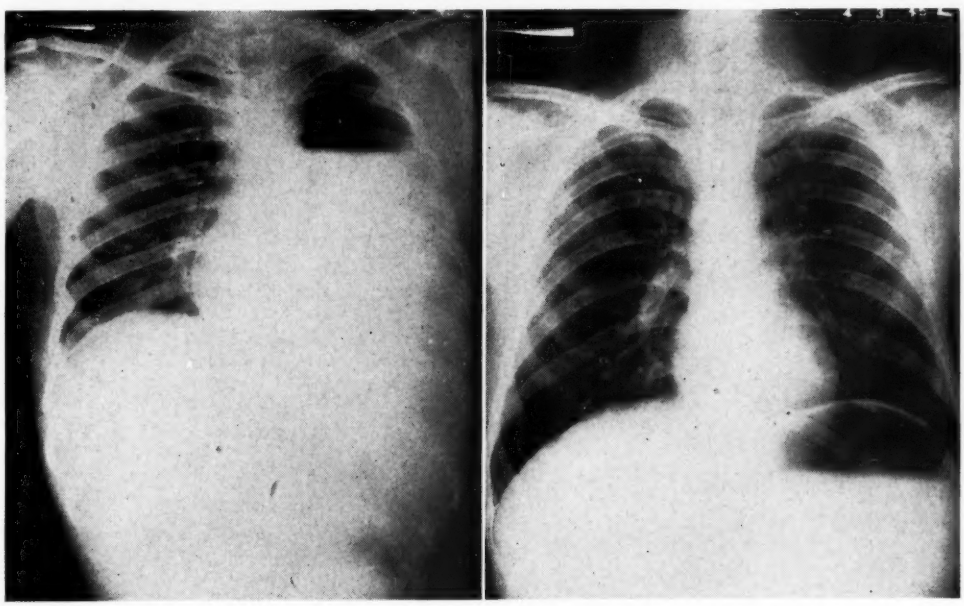
at one thoracentesis. The procedure was repeated every day or two until the lung was re-expanded as completely as possible.

The advantages of obtaining early re-expansion of the lung are (1) to avoid the residual changes in the pleura, (2) to speed up the convalescence, and (3) to decrease the size of an empyema should infection occur. The objection to removing the blood from the pleura and replacing it with air is, of course, that it leaves the lung collapsed and increases the size of the empyema should infection occur.



A. *B.*

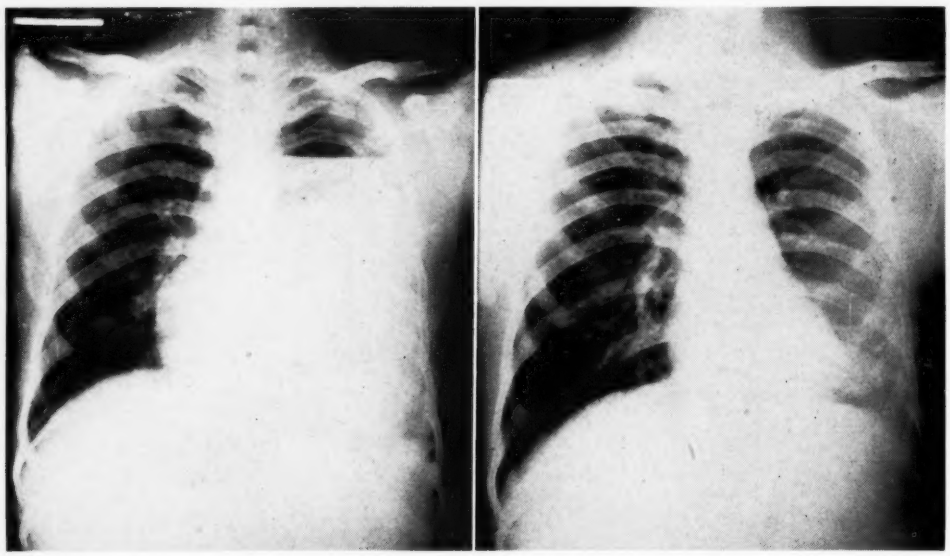
Fig. 1.—*A*, A 25 caliber bullet perforated the left side of the chest of an American officer forty-eight hours before this roentgenogram was taken. He was not severely dyspneic. *B*, A total of 2,000 c.c. of bloody fluid was removed by three thoracenteses. This view was taken one week later, or nine days after he was wounded. Physical examination showed the lungs to be clear. He made a rapid recovery.

Pneumothorax.—Occasionally a patient was seen who had a pneumothorax with little or no blood in the pleural cavity. Here too it was learned that early re-expansion of the lung was desirable. If the pneumothorax was gradually increasing in size, it would often be controlled by repeated thoracenteses. The opening in the lung usually closed after a few days and thoracentesis resulted in complete re-expansion of the lung. A pneumothorax apparatus was often found to be helpful in these cases.

In the presence of a real tension pneumothorax which reaccumulates rapidly after thoracentesis, there should be no hesitancy in introducing a catheter into the pleural cavity to allow the continual escape of air. In no patient in this series was it necessary to suture a tear in the lung because of persistent pneumothorax. In one patient, however, while the inter-rib catheter relieved the tension pneumothorax, the associated subcutaneous emphysema continued. It became apparent that the air was escaping into the mediastinum from the

tracheal wound incident to the great increase in the intratracheal pressure which occurred during coughing. Simple tracheotomy prevented the building up of a high intratracheal pressure during coughing and the emphysema disappeared progressively thereafter.

Clotted Hemothorax.—Decortication of the lung in the presence of a clotted hemothorax was first used extensively in the Mediterranean Theater under the supervision of Churchill.[1] Speaking as one who treated several of these patients conservatively early in the war, I am certain that they are left with a fibrothorax which considerably reduces the functional capacity of the thorax.



A. *B.*

Fig. 2.—*A*, Roentgenogram taken one week after the left side of the chest of a Chinese soldier was perforated by a 25 caliber bullet. He was not severely dyspneic. He was treated conservatively without thoracentesis. *B*, The fluid in the chest disappeared very slowly. This view was taken six weeks later. It shows only moderate thickening of the pleura. However, physical examination revealed marked limitation of motion on that side with markedly decreased breath sounds. His convalescence was prolonged.

Early decortication of the lung as practiced in these patients is now accepted by all who had the opportunity of caring for thoracic injuries. When operation is performed in the first few weeks, the liquid blood and exudate may first be removed leaving behind a fibrinous layer of tissue covering the surface of the partially collapsed lung. This layer of tissue may then be peeled from the lung surface, thereby permitting immediate complete re-expansion of the lung.

Infected Hemothorax—Acute Empyema.—Early in the war, I treated empyemas in the conventional manner. I did repeated thoracenteses to re-expand the lung as much as possible until the pus was thick enough to assure fixation of the lung and mediastinum in the presence of an open thoracostomy. I was not satisfied with the rather slow re-expansion of the lung obtained by open drainage. Early closed drainage was then used in some patients because it offered the advantage of possible application of suction and, thus, assistance in

the more rapid re-expansion of the lung. On the other hand, the amount and viscosity of the exudate in many patients obstructed the inter-rib catheter and made the suction ineffectual.

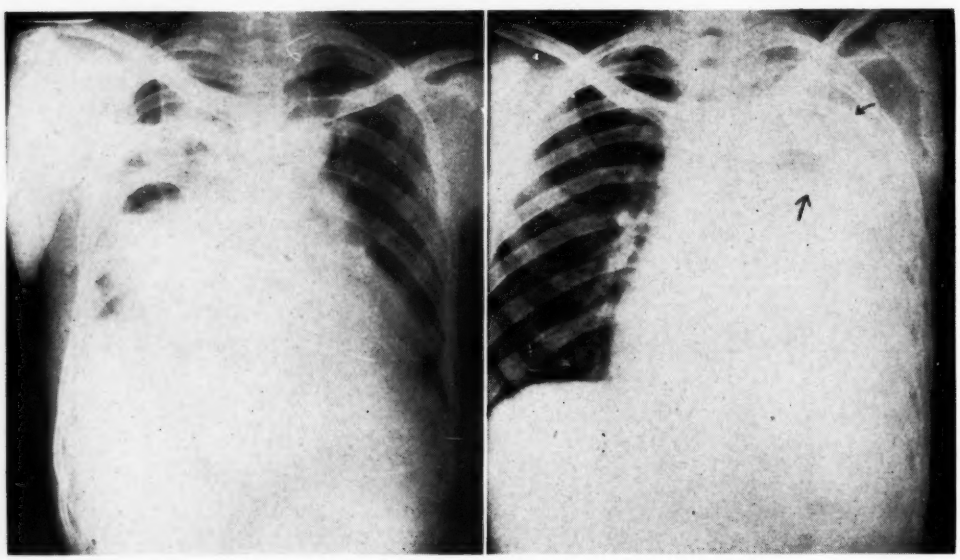
A method was then devised which provided the advantages of both open and closed drainage. A large opening was made in the chest wall by taking out sections of two ribs, and all the exudate was cleaned out. In order to re-expand the lung more rapidly the open drainage was then reconverted into a closed

Fig. 3.—A Chinese soldier had a tension pneumothorax on the right side with marked mediastinal and subcutaneous emphysema. The subcutaneous emphysema extended from above the ears, to the backs of the fingers, and halfway down the thighs. The tension pneumothorax was relieved by an inter-rib catheter. The subcutaneous emphysema continued to increase upon coughing. The course of the bullet indicated that the mediastinal trachea had probably been perforated. A tracheotomy was done to prevent the tremendous increase in intratracheal pressure upon coughing. The subcutaneous emphysema decreased progressively thereafter.

system, using the airtight seal demonstrated in Fig. 5. The idea of using wide exposure first was to remove the exudate completely. A ¾ inch rubber tube was used for drainage which was not easily plugged by exudate. Using a high degree of negative pressure (100 to 150 cm. of water) it was found that the lungs re-expanded much more rapidly than would have occurred by simple open drainage or by closed drainage as commonly used.

Having become confident of being able to convert an open thoracostomy into a closed one, I then began to operate upon infected hemothoraces as soon

as the diagnosis was made. Intratracheal anesthesia was used and a large opening was made as described. The blood and exudate were removed, although decortication of the lung was not done. The latter, while already adopted in the Mediterranean Theater of Operations, had not come to my attention. At this early stage, however, the layer of fibrinous exudate over the lung was quite thin so that when a high degree of negative pressure was applied the lung re-expanded rapidly. When the pleural space had been reduced to the size of the large tube, a smaller tube was inserted and suction continued. Suction was continued until the cavity measured less than 5 c.c. During the Central Burma Campaign decortication of the lung was added to this procedure. A large (¾ inch) rubber tube and a high degree of suction continued in use, care being taken that the pleural space was completely obliterated before removing it.

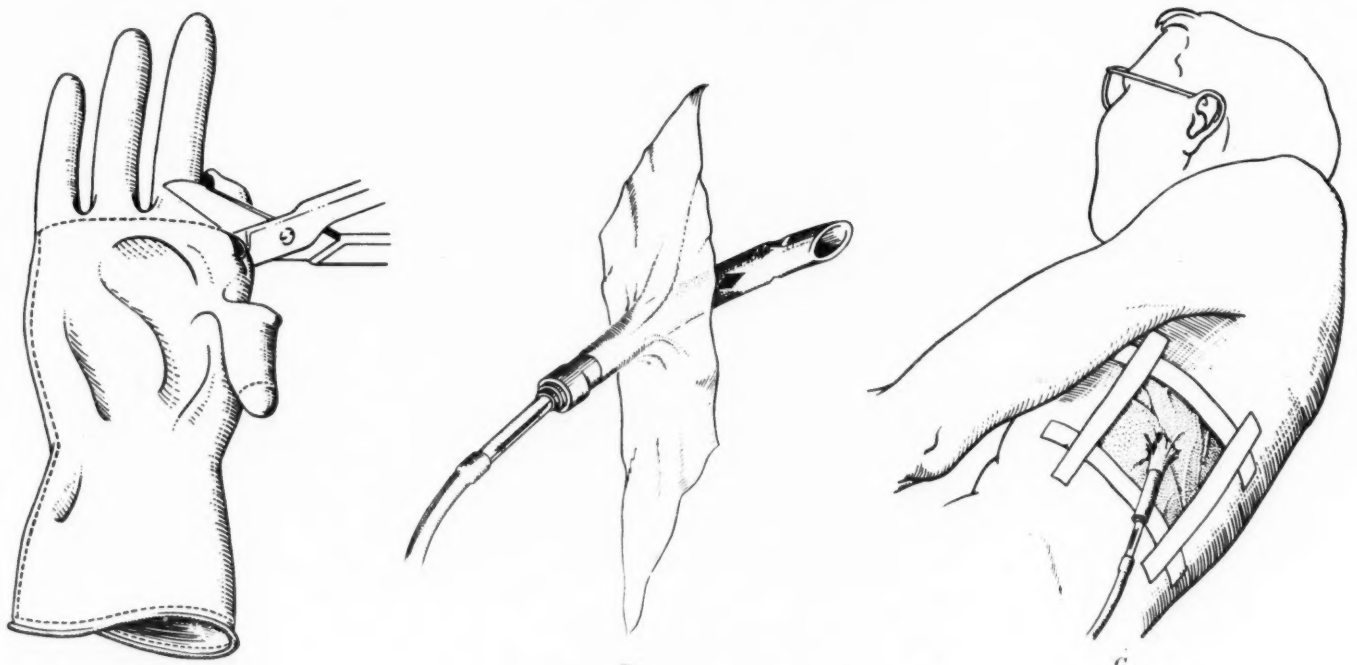


A. *B.*

Fig. 4 *A* and *B*.—Two examples of clotted hemothorax. *A* has multiple fluid levels while *B* has only two small fluid levels which are not easily seen. Only a small amount of fluid could be obtained by thoracentesis in either case. These represent the type of clotted hemothorax which responds well to decortication as has been demonstrated in every theater of the war. When left alone a partially disabling fibrothorax develops.

Burford, Parker, and Samson[2] have reported twenty-five patients with infected hemothorax upon whom decortication was performed. They obtained good results. It was their practice to use a drainage tube for only a few days, so that six patients developed secondary basal empyema and required secondary operation. Perhaps this could have been avoided by using a large tube with suction as was done in our case. Decortication in these early cases of empyema has now been fairly widely used.[5, 6]

Infected Open Sucking Wounds.—Occasionally a patient was seen in the rear echelon whose sucking chest wound had been sutured in the forward area but had broken open to become sucking again. Because of the loss of tissue and the presence of infection it may have been impossible or inadvisable to close the chest wall. Here the problem is one of obtaining re-expansion of the lung

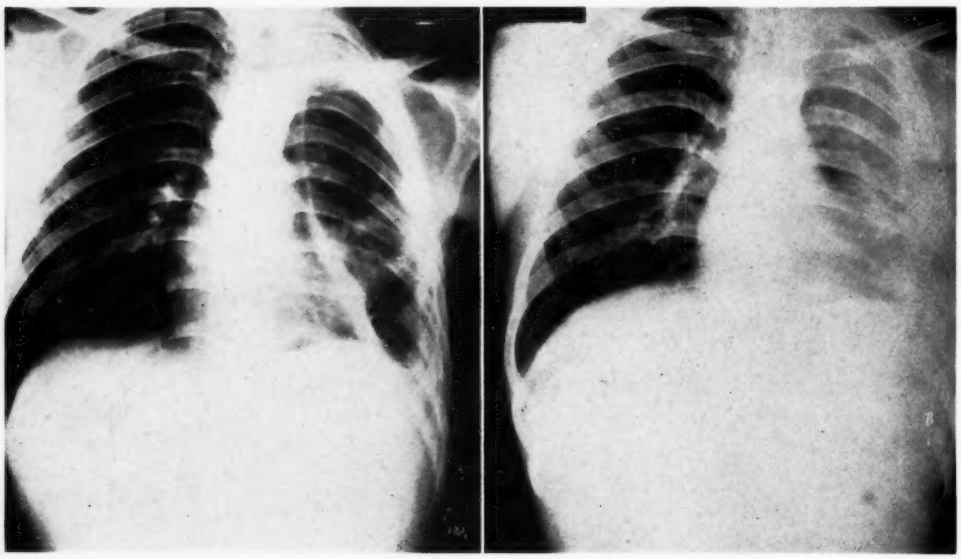


A. *B.* *C.*

Fig. 5 *A-C.*—The re-expansion of the lung following open thoracostomy was hastened by means of an airtight seal and suction of 100 to 150 cm. of water by means of a Wangensteen three-bottle suction apparatus. *A*, The fingers were cut from a rubber glove. The tip of the thumb was cut away and the glove was cut down the ulnar side. *B*, The glove was then opened and a large (¾ inch) rubber tube placed through the thumb. The thumb was glued to the rubber tube. *C*, The outstretched glove was then glued to the skin around the wound with the glue used with the Padgett dermatome. Suction was applied at once.

rather than of closing the chest wall wound. In three such patients the open wound was converted into a closed thoracostomy by means of the airtight seal previously described. In two of these patients the lungs re-expanded rapidly, became adherent, and the final results were excellent. In the third patient a bronchopleural fistula temporarily delayed re-expansion, but later complete re-expansion was obtained.

Chronic Empyema.—Decortication of the lung for chronic empyema has been used occasionally for many years.[3, 4] Before the advent of chemotherapy, however, most surgeons feared the dangers of spreading infection. Up until this war, as a rule, the patient with chronic empyema whose lung would not re-expand completely was subjected to a destructive operation in order to obliterate the remaining cavity.

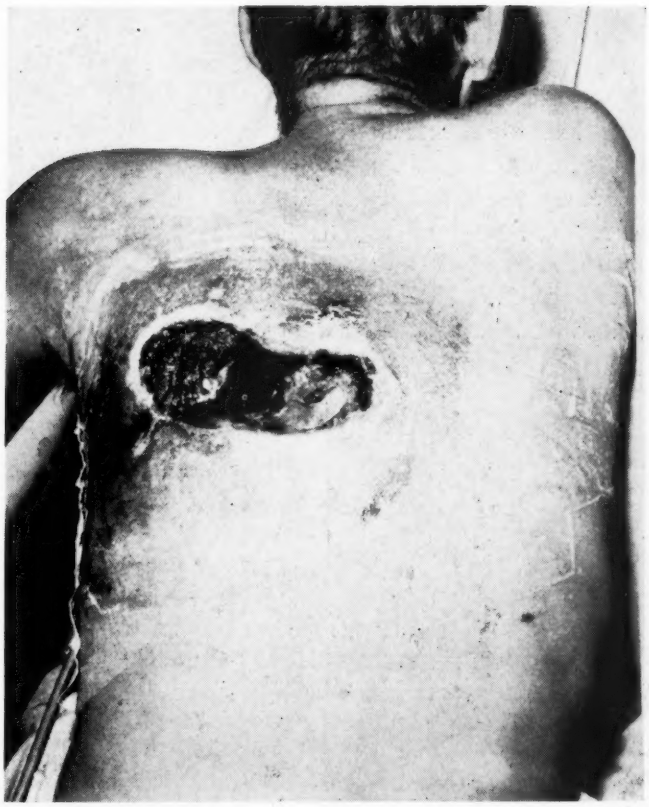


A. *B.*

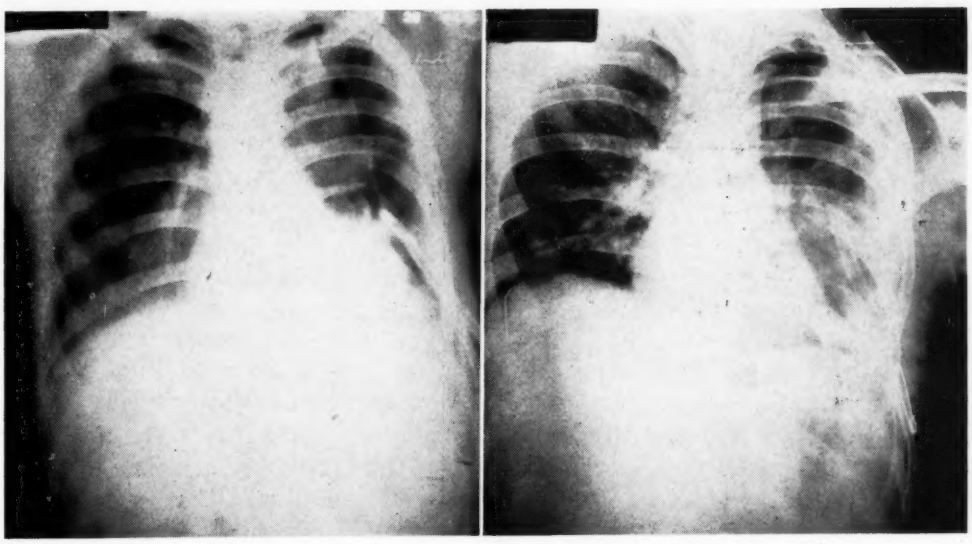
Fig. 6.—*A*, A Chinese soldier, two months after being wounded, with an open empyema and almost total collapse of the lung. *B*, Suction of 150 cm. of water was applied by the method shown in Fig. 5. Within a period of one month complete re-expansion of the lung had been obtained.

Decortication of the lung as popularized in this war was suggested primarily for early cases. The procedure has been used widely and in most instances has given excellent results. Kay and Meade[6] have noted that the results were much better when the pleura was drained. As we gained confidence in being able to carry out the mechanical aspects of decortication, and with the aid of chemotherapy to help prevent spreading infection, it was inevitable that late decortication should be attempted.

During the Central Burma campaign a British soldier came under my care with a four-month-old empyema and total collapse of the left lung. Since the alternative was a total thoracoplasty, decortication was carried out. The result was very satisfactory (Fig. 8). A layer of fibrous tissue covering the lung was tightly adherent to the surface of the lung and in places had to be separated from it by sharp dissection. Inevitably several openings were made in the lung. The



A.

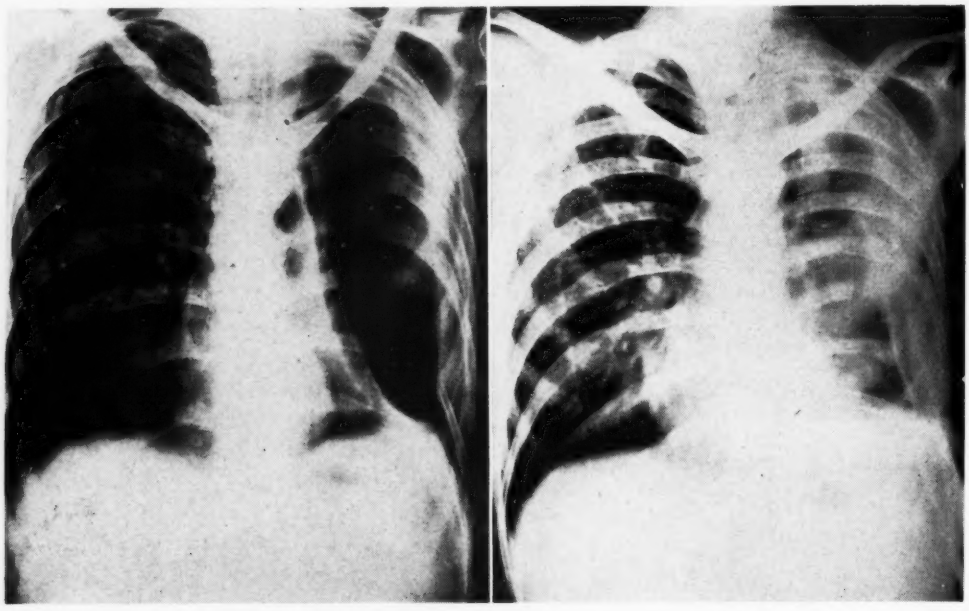


B. *C.*

F.g. 7.—*A*, The wound of this soldier had been sutured in the forward area but he developed gas gangrene and the wound opened, becoming "sucking" again. Because the wound could not be resutured, the dead tissue was excised and the chest wall sealed by the method shown in Fig. 5. A catheter was also placed low in the chest. *B*, Because of a small bronchopleural fistula the lung could not be re-expanded immediately. About 10 cm. of water of negative pressure were maintained. *C*, After about one week the bronchopleural fistula closed and the lung became completely re-expanded, when about 150 cm. of water of negative pressure were applied.

larger tears were sutured but there were still multiple small leaks. A large rubber tube (¾ inch) was used for drainage under water. Suction was applied once each day to determine whether the multiple small bronchiopleural fistulas had closed. A Wangensteen suction apparatus was used. For the first three days the bronchiopleural fistulas remained open. On the fourth day there was no longer any leak and the lung rapidly became completely re-expanded.

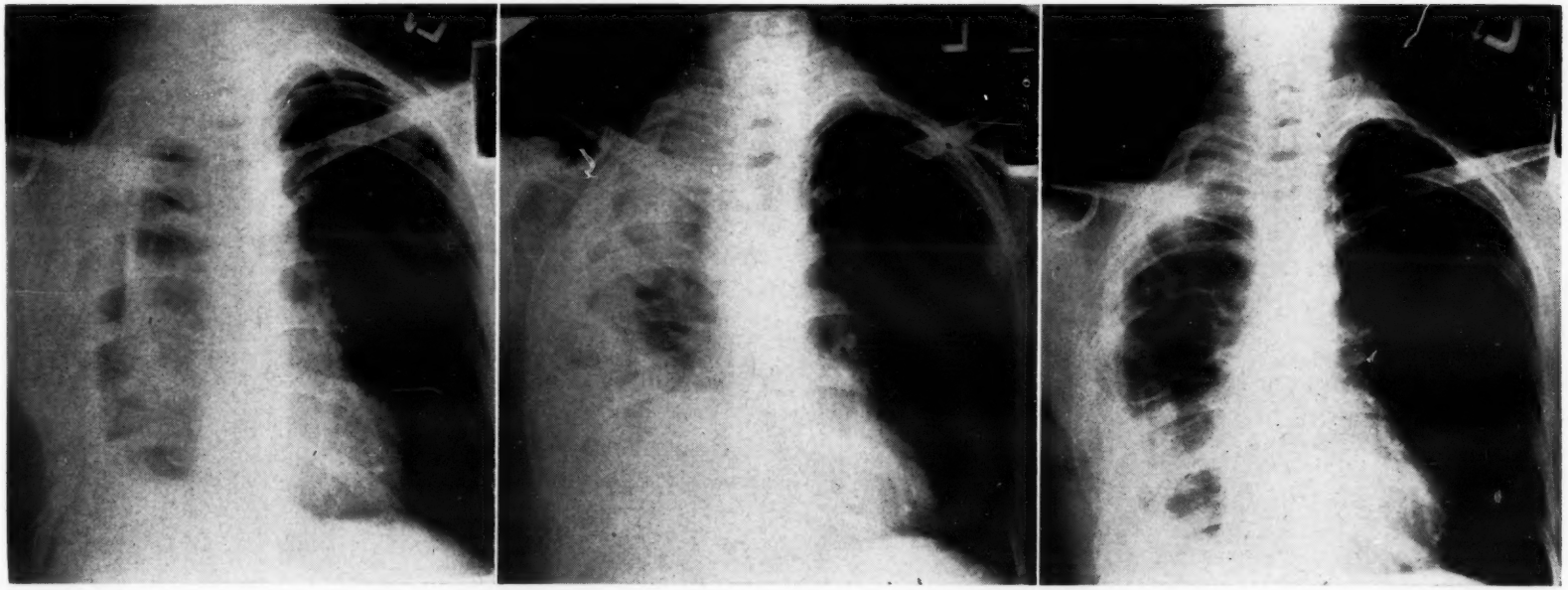
Upon return to the United States I found that Lt. Col. Brian Blades and his associates at the Walter Reed General Hospital had been doing decortication in late empyemas and had been successful as late as eight months following the original injury.



A. *B.*

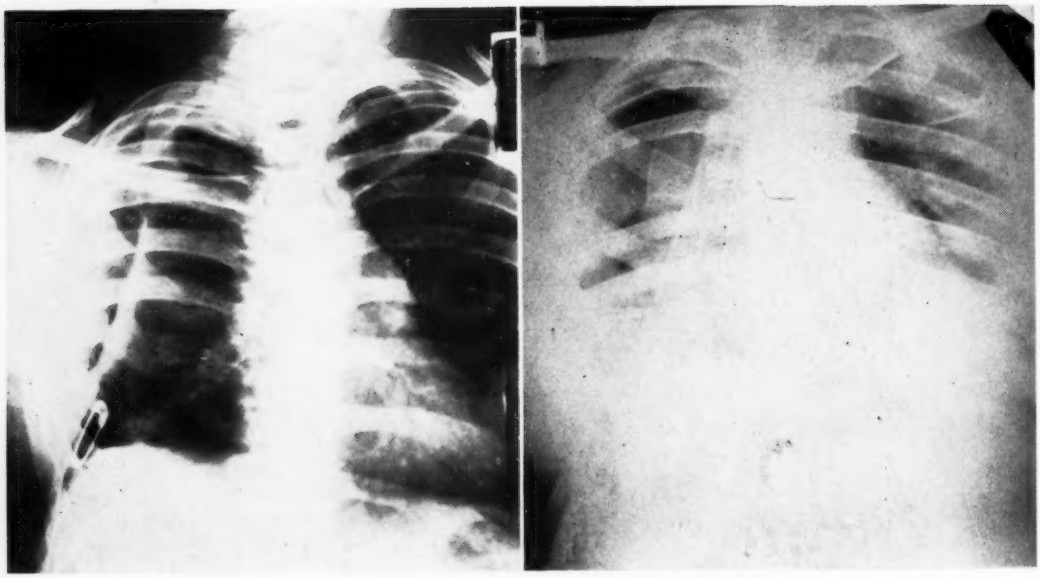
Fig. 8.—*A*, A British soldier, four months after being wounded, with almost a total collapse of the left lung. *B*, Decortication of the lung was performed. The thickened parietal pleura was not removed. Several holes were made in the lung by the decortication, so that although the lung could be expanded at operation it could not be maintained in the expanded state. These small leaks sealed on the third day and the lung re-expanded completely. The roentgenogram was taken five days after operation, showing complete re-expansion. The large tube with suction was left in place for about two weeks to be certain that the pleural cavity was obliterated.

At the Thoracic Surgical Center at the Kennedy General Hospital where I was assigned following my return to this country, two men came under my care who had chronic empyemas with considerable collapse of the lung one year after injury (Figs. 9 and 10). In each there was present very thick pleura with empyema cavities of about 150 to 200 c.c. It was obvious that any type of thoracoplasty would result in considerable deformity and in a reduction of functional capacity of the lung. In each instance decortication with re-expansion of the lung was possible. Again a number of lacerations of the lung surface occurred but these became closed in a few days. By the use of high degrees of negative pressure, the lungs were completely re-expanded. Since it was not possible to close the original drainage wound around the tube, the airtight seal described here was helpful in both cases.

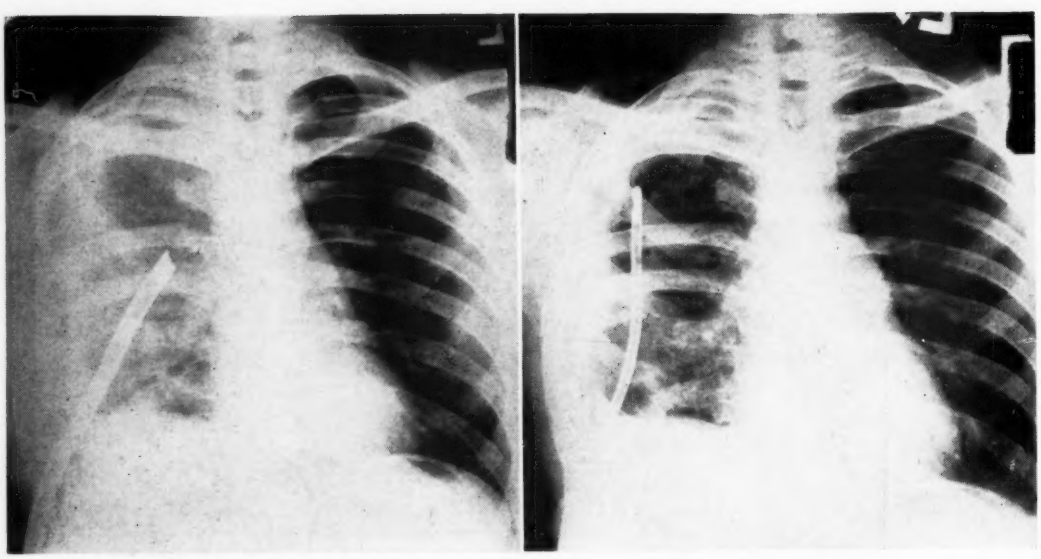


A. *B.* *C.*

Fig. 9.—*A*, A soldier wounded more than one year previous to this x-ray examination. He started out with almost complete collapse of the lung. It gradually re-expanded to the present state. As can be seen the parietal pleura is very thick. The free pleural cavity measured about 150 c.c. There had been no improvement for the past few months. *B*, A decortication of the lung was performed. The thickened parietal pleura was also removed. Because of multiple small leaks in the lung, immediate complete re-expansion of the lung was not obtained. In this instance, as can be seen, there was some clotting of the fluid in the chest in spite of the application of suction. *C*, By the use of high degrees of suction through the large (¾ inch) tube which was changed frequently, the lung was re-expanded and the pleural cavity completely obliterated. At this time, one month after operation, the cavity was only the size of the tube.



A. *B.*



C. *D.*

Fig. 10.—*A*, A soldier wounded more than one year prior to this x-ray examination. He also had had a total collapse of the lung which had gradually re-expanded. It had made no progress for several months. There was a thick parietal pleura. The cavity measured 180 c.c. *B*, Decortication of the lung was performed. The thickened parietal pleura was also removed. This view was taken the day after operation. Because of multiple small tears in the lung it could not be re-expanded immediately. *C*, The holes in the lung sealed on the fourth day and the lung re-expanded. *D*, Three weeks later the lung was completely re-expanded. At this time the cavity held only 3 c.c. of fluid in addition to the tube. The tube was then gradually shortened and removed.

We are aware that decortication in these late cases has not always been successful in other hands. Moreover, it will probably not always be successful in our hands. However, if considerable care to detail is exercised when handling these patients, it is believed that success will be attained in most instances. Certainly an attempt to re-expand the lung is justified in those patients in whom considerable thoracoplasties would be required to obliterate the cavity. We believe that it is important to use a large rubber tube (¾ inch) to decrease the danger of its becoming plugged, and to apply a high degree of negative pressure to facilitate re-expansion of the lung, once the small lacerations in the lung surface have become sealed.

Should decortication be done in the presence of a chronic bronchopleural fistula, it would probably be advisable, I believe, that the decortication be complete around the fistula and that the fistulous wall be excised deep into the lung so that normal lung tissue can be closed by suture.

SUMMARY

The fundamental objective in the treatment of battle wounds of the thoracic cavity should be early and complete re-expansion of the lung.

1. Hemothorax is best treated by early repeated thoracentesis to re-expand the lung as completely as possible.

2. Pneumothorax may be treated by early re-expansion with a pneumothorax apparatus. An inter-rib catheter is advisable in the patient with severe tension pneumothorax.

3. Clotted hemothorax should be treated by decortication of the lung with complete re-expansion within the first few weeks.

4. Acute empyema—infected hemothorax may be treated by early decortication and re-expansion of the lung. A large drainage tube with the use of suction is helpful.

5. Sucking wounds of the chest which cannot be closed because of loss of tissue and infection may be handled by means of an airtight seal and suction to re-expand the lung.

6. Chronic empyema with considerable collapse of the lung should be treated by decortication and re-expansion of the lung. The use of high degrees of suction (100 to 150 cm. of water) through a large rubber tube (¾ inch) has been helpful in our experience. The airtight seal described herein may be very useful in those patients in whom it is difficult to close the original drainage wound around the tube. Considerable attention to detail is required in these cases.

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ALTERATIONS OF THE BLOOD FOLLOWING INTRATHORACIC OPERATIONS

A Clinical Study

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(From the Department of Surgery of the University of Chicago)

SEVERAL studies have shown the extent of blood loss in thoracic operations. White and Buxton,[1] in 1942, by direct measurement estimated a 700 c.c. blood loss with each stage thoracoplasty and an average of approximately 1,500 c.c. with pneumonectomy and lobectomy. They advised large transfusions during operation, emphasizing that the extent of blood loss was not generally appreciated. Other blood loss estimates including those of workers[2] in this laboratory who used blood volume methods have shown comparable results. As a consequence of such studies it is now becoming an established practice in extensive surgery to give preoperative transfusions to the patient if anemia or hypoproteinemia is present, to replace blood as it is lost during operation, and to give postoperative transfusions to the patient as indicated by his clinical state and blood picture. However, the determination of how much replacement therapy is necessary is difficult; indeed, surgical shock may occur before the surgeon realizes that circulating fluid loss has been severe. Coller and his co-workers,[3] in an excellent review of blood loss in surgical operations, concluded that direct measurement is necessary in order to know the exact amount of blood loss and therefore the exact amount of blood to replace. However, direct measurement of blood loss is often not practical and the surgeon must rely on knowledge of average losses, the clinical state of the patient and the results of routine blood examinations, the red cell count, the hemoglobin estimation, plasma protein concentration, and the hematocrit.

To assume that there is quantitative relationship between the changes in the hemoglobin, plasma proteins, or hematocrit and the amount of blood loss and using these as a measure for fluid replacement is fallacious as was pointed out by Stewart and Rourke[4] in 1938. However, Ebert, Stead, and Gibson[5] in 1941, studying the response of normal subjects to acute blood loss, reported that the hematocrit readings accurately reflected the direction of changes in plasma volume. Thornton, Adams, and Schafer[6] in this laboratory in 1944 studied plasma protein changes after intrathoracic operation but mentioned that they were unable to correlate entirely hematocrit determinations with the drop in plasma proteins. However, twenty-one of the twenty-nine patients showed postoperative fall in hematocrit and they concluded that replacement therapy must have been inadequate although every effort was made to replace

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with whole blood the exact amount of the estimated loss. It was also noted that the fall in plasma proteins as well as the hematocrit, hemoglobin, and to a lesser extent the red cell count occurred from the third to fifth day following operation. For these reasons it was felt that a careful study of changes in the red cell count, hematocrit, hemoglobin concentration, and blood volumes before and after major thoracic operations might be valuable especially as to their indicating the adequacy or inadequacy of replacement therapy.

METHODS OF STUDY

Repeated erythrocyte counts, and hematocrit and hemoglobin determinations were made pre- and postoperatively in nineteen patients, with seventeen intrathoracic operations and two thoracoplasties. In five of these patients plasma volume and total blood volume determinations were made before and after operation. In all patients, with one or two exceptions, the aim was to replace with whole blood the blood loss as estimated by the surgeon. Patients who showed marked hypoproteinemia or anemia were prepared for operation by preoperative whole blood and plasma transfusions. Blood transfusion was carried on during the operation except in one or two patients and postoperative transfusions were given whenever indicated by the state of the patient or in the face of moderate to severe anemia. The studies were conducted in the following manner. Erythrocyte counts, and hemoglobin and hematocrit determinations were made before operation on all patients. In those patients receiving preoperative transfusion therapy several such determinations were done. In the first five patients daily hematocrit, erythrocyte, and hemoglobin determinations were made until the patient was discharged or preoperative levels were reached and maintained. From these data it was found that erythrocyte counts and other determinations on alternate days were sufficient. In addition to these determinations, plasma volumes were done in five patients: the first determination preoperatively, the second within three hours after the patient had returned from the operating room, and a third determination seven to twelve days following surgery.

Hemoglobin estimation was done by the macro-tube oxyhemoglobin method of Evelyn[7] using the photoelectric colorimeter. Hematocrits were done by the method of Van Allen[8, 9] and erythrocyte counts were made in the usual manner. All blood samples were obtained by venipuncture with a minimum of venostasis. The anticoagulant used was heparin. Plasma volumes were determined by the Evans' blue dye (T 1824) technique as described by Gibson and Evans[10] and adapted to the photoelectric colorimeter by the micromethod of Gibson and Evelyn.[11] Slight modifications in the method of standardizing the dye and in determining plasma volume were suggested by Schafer[12] of this department. The operations on the nineteen patients studied are classified in Table I.

Two patients had inoperable carcinoma of the lung and one patient had inoperable carcinoma of the cardia extending to the lower esophagus. One patient with extensive carcinoma of the esophagus died on the twenty-seventh postoperative day of peritonitis; one with carcinoma of the cardia died on the

TABLE I. CLASSIFICATION OF OPERATIONS IN NINETEEN PATIENTS

OPERATION		NUMBER
Lobectomy		6
Left lower lobe and lingula	4	
Right lower lobe	2	
Pneumonectomy		3
Exploratory thoracotomy		1
Exploratory thoracolaparotomy		2
Transthoracic vagotomy		2
Miscellaneous		5
Resection part of esophagus and esophagogastrostomy	2	
Thoracoplasty	2	
Resection of 3 ribs and part of chest wall and exploratory thoracotomy	1	
Total		19

eleventh postoperative day of myocardial infarction; and a third patient with carcinoma of the lung died of bronchial asthma and right heart failure on the second day. All other patients had satisfactorily recovered from the operations by the time the study was completed. Pertinent data on the patients are given in Table II.

The patients are grouped in this table according to the type of operation following the classification given above. Under each of the major headings is listed the hemoglobin in grams per cent, the hematocrit showing percentage of red cell mass in whole blood samples, and the erythrocyte count in millions per cubic millimeter. Under each of these is listed the preoperative status, the lowest postoperative level, the amount of this fall, and the day on which this greatest change was found. Also under the heading, Day Return is listed the day on which postoperative determinations showed return to preoperative levels or, as in many instances where preoperative levels were not reached, the last determination before the study was concluded. In every case these determinations were not discontinued until the blood picture had been stabilized for several days or the patient had been discharged. In many cases complete recovery to preoperative levels had not occurred even though two to three weeks had elapsed. The amount of blood or plasma transfusion is listed as it was given preoperatively, postoperatively, or at the time of the operation. Circumstances which might have significant effect on the blood picture, such as postoperative hemorrhage, infection, or secondary disease, are listed under appropriate columns. Under the group of lobectomy patients averages have been made since the group was sufficiently large and changes sufficiently uniform to make these figures meaningful.

RESULTS

At time of operation nine patients had hemoglobin levels of less than 85 per cent of normal (13.26 Gm. per cent) but of these only four had less than 80 per cent (12.48 Gm. per cent). Fifteen and six-tenths grams of hemoglobin per 100 c.c. of blood are arbitrarily taken as 100 per cent. Of these four, one (J. N.) was given a 500 c.c. whole blood transfusion five days before operation because the initial blood determination showed only 10.06 Gm. per cent hemoglobin and a hematocrit of 32.5 per cent. This transfusion effected little change in

the hemoglobin or hematocrit as can be seen from preoperative status in Table II; however, the patient's symptom of severe weakness was improved. He had had marked symptoms and a twenty-eight pound weight loss in the past year.

Two other patients were given preoperative transfusion. D. O. (see Graph 3), an 8-year-old boy with congenital cystic disease of the lung and symptoms for about one year, had an initial hemoglobin of 8.6 Gm. per cent and a hematocrit of 29.6 per cent. Three 300 c.c. whole blood transfusions in the twenty days before operation resulted in marked improvement of the blood status, the hematocrit going to 41.5 per cent and the hemoglobin to 13.4 Gm. per cent. G. A. (Graph 5) had had a cholecystectomy nineteen days previous to the operation in this study and he was given 450 c.c. of whole blood two days before this study started. Hemoglobin at the time of operation was 13.2 per cent.

Thornton, Adams, and Schafer[6] have mentioned the rather surprising observation in a study of hypoproteinemia in thoracic surgery that few patients had marked hypoproteinemia although chronic infection and carcinoma were the most common diseases. In this group of similar patients we can make such a statement regarding grams per cent of hemoglobin; namely, only six patients out of nineteen had less than 80 per cent hemoglobin (12.48 Gm. per cent) on initial examination and, as mentioned previously, only four patients had less than 12.48 Gm. per cent at the time of operation. This is in contrast to the results of blood status studies in patients with carcinoma or chronic infection in other parts of the body. For example, Oppenheim and associates[13] reported 64 per cent of patients with carcinoma of the stomach as having abnormally low red cell counts and hemoglobin concentration. It has long been known that there are compensatory changes in the percentage of hemoglobin or red cells in the blood when the oxygen transport capacity of the lung is decreased. Chronic lung disease may therefore account for the fact that most of these patients had a blood status above the anemic level.

In the six patients on whom lobectomies were done the average postoperative fall in the hemoglobin estimation was 2.1 Gm. per cent and the average of the days on which this lowest fall was found was 5.2 days. The range was .6 to 4.0 Gm. and three to eight days. This is approximately true for all the patients in this series, although in general the patients with first stage thoracoplasty and those in whom there was extensive resection, as in Patient C. K., the drop in gram per cent of hemoglobin was somewhat greater. Only one patient, J. N., showed no fall after operation and he was given 1,600 c.c. whole blood during operation, which was considered more than adequate replacement of the estimated blood loss.

In only two patients in the series had the preoperative hemoglobin level been reached by fourteen days postoperatively; one of these was J. N., in whom no drop occurred, and the second, B. G. (see Graph 2), maintained this level of hemoglobin for only one week, then it again dropped below preoperative levels during the final week before she died on the twenty-seventh day.

Although the average day of lowest hemoglobin determination in the lobectomy patients is 5.2, it was observed that the greatest per cent of this

fall occurred in the period between the first and third days after the operation. A relatively small percentage of the average fall occurred in the first twenty-four hours or in the period from the third to the fifth day. Four patients even showed hemoglobin estimates at or better than preoperative level twenty-four hours after the operation. From this one would think the blood loss during operation was more than adequately replaced during the operation. However, with one exception, all of these patients later, usually by the third to the fifth day, showed drops in hemoglobin below preoperative levels and in the case of the lobectomy patients this amounted to 2.1 Gm. per cent or approximately a drop of 12.5 per cent.

The average fall in hematocrit in the lobectomy patients was 7.0 per cent and the average day on which the lowest level was reached before starting to

TABLE II. ALTERATION OF THE BLOOD FOLLOWING

PATIENT, SEX AND AGE	DIAGNOSIS	OPERATION	INFECTION	WHOLE BLOOD TRANSFUSION	REMARKS
					Lobectomy
1. F. W., M., 32	Bronchiectasis	Left lower lobectomy and lingulectomy	–	1,000 c.c. at operation	
2. D. O. M., 8	Congenital cystic disease	Left lower lobectomy and lingulectomy	–	900 c.c. before operation, 1,200 c.c. at operation, ? after operation	
3. G. H., F., 39	Pulmonary suppuration	Right lower lobectomy	–	1,000 c.c. at operation, 500 c.c. after operation	
4. L. C. V., F., 17	Congenital cystic disease	Right lower lobectomy	–	1,800 c.c. at operation	
5. C. F., M., 30	Bilateral bronchiectasis	Lower left lobectomy and lingulectomy	–	1,000 c.c. at operation	
6. M. N., M., 18	Bronchiectasis	Lower left lobectomy and lingulectomy	–	1,000 c.c. at operation	Mild diabetes mellitus
Average				1,167 c.c. at operation	
					Transthoracic
1. G. P., M., 49	Ulcer, recurrent	Transthoracic vagotomy	–	0	
2. M. S., M., 45	Stomal ulcer, recurrent	Transthoracic vagotomy	–	0	

*Detailed studies of the blood following intrathoracic operations in nineteen patients. In the columns to the left are given the diagnosis, the type of operation, and the amount of whole blood transfusions received. In the columns to the right are indicated the hemoglobin, hematocrit, and erythrocyte values prior to and following operation. The amount of fall, and the day on which it was greatest, is indicated, as well as the time when the blood picture returned to normal.

return toward preoperative levels was 4.6 days. The range was 3.9 to 12.9 per cent and three to seven days. The changes in hematocrit both in percentage of change and the day on which the change occurred almost exactly parallels changes in hemoglobin.

The average fall in erythrocyte counts in the six lobectomy patients was .95 million and the lowest counts were registered on an average of 4.8 days. This roughly parallels the hemoglobin and hematocrit changes, but it is observed from the graphs that the red cell count is frequently erratic (see Graphs 1 and 2) and often shows daily variations which are not in accord with the percentage or even the direction of change of the hemoglobin and hematocrit. Graphs of the blood status show that in more than one-half of the patients the red cell count more nearly approached 100 per cent (5.00 million equals 100 per cent)

INTRATHORACIC OPERATIONS IN NINETEEN PATIENTS*

HEMOGLOBIN (GM. %)					HEMATOCRIT (% OF TOTAL BLOOD)					ERYTHROCYTE COUNT (MILLIONS PER CU. MM.)				
PRE-OPERATIVE	FALL	POST-OPERATIVE	DAY FALL	DAY RETURN	PRE-OPERATIVE	FALL	POST-OPERATIVE	DAY FALL	DAY RETURN	PRE-OPERATIVE	FALL	POST-OPERATIVE	DAY FALL	DAY RETURN
(6)														
14.8	2.4	12.4	6	12.53 on Day 13	42.9	6.0	36.9	7	38.7 on Day 13	5.10	1.2	3.90	3	4.63 on Day 13
13.4	4.0	9.4	8	11.96 on Day 15	41.5	12.9	28.6	4	35.8 on Day 15	5.10	1.4	3.70	4	4.55 on Day 15
11.3	1.9	9.4	3	11.1 on Day 12	35.3	5.4	29.9	3	35.8 on Day 12	4.27	.28	3.99	4	4.41 on Day 12
12.9	1.6	11.3	4	11.7 on Day 13	39.5	6.0	33.5	4	34.4 on Day 13	4.77	1.29	3.48	8	3.95 on Day 13
14.1	2.1	--	--	12.0 on Day 12	42.4	7.5	--	--	34.9 on Day 12	4.70	.56	--	--	4.14 on Day 12
15.7	.6	15.1	5	14.9 on Day 10	46.6	3.9	42.7	5	43.5 on Day 10	5.82	.97	4.85	5	4.97 on Day 10
13.50	2.1	11.4	5.2	12.37 on Day 12.5	41.2	7.0	34.2	4.6	37.2 on Day 12.5	4.96	.95	4.01	4.8	4.44 on Day 12.5
Vagotomy (2)														
17.6	4.2	13.4 day of operation	--	13.7 on Day 9	53.3	12.7	40.6 day of operation	--	35.4 on Day 9	6.40	1.69	4.71 day of operation	--	4.42 on Day 9
14.4	1.5	13.9 day of operation	--	10.4 on Day 9	44.8	5.3	39.5 day of operation	--	30.7 on Day 9	5.28	.79	4.51 day of operation	--	3.84 on Day 9

TABLE II

PATIENT, SEX AND AGE	DIAGNOSIS	OPERATION	INFECTION	WHOLE BLOOD TRANSFUSION	REMARKS
					Miscellaneous
1. B. G., F., 62	Carcinoma of esophagus	Resection of lower ⅔ of esophagogastrostomy and splenectomy	Yes	1,500 c.c. at operation	Patient died of peritonitis 27 days P.O.
2. I. W., M., 68	Carcinoma of cardia	Esophagogastrostomy	No	1,500 c.c. at operation	Patient died of myocardial infarction on 11th day P.O.
3. M. W., F., 41	Pulmonary tuberculosis	Thoracoplasty, Stage I	No	500 c.c. at operation, 500 c.c. on 4th P.O. day	Patient had severe hemorrhage into wound immediately after operation
4. H. C., F., 41	Pulmonary tuberculosis	Thoracoplasty, Stage I	No	1,000 c.c. at operation	----------
5. C. K., M., 55	Carcinoma of lung extending to chest wall	Resection of 3 ribs and exploratory thoracotomy	No	1,000 c.c. at operation	----------
					Pneumonectomy
1. J. N., M., 64	Carcinoma	Pneumonectomy of right lung	No	500 c.c. before operation, 1,600 c.c. at operation	----------
2. M. B., F., 45	Sarcoma	Pneumonectomy of left lung	No	1,000 c.c. at operation	----------
3. H. W., M., 54	Carcinoma	Pneumonectomy of right lung	No	1,500 c.c. at operation	Died on 2nd P.O. day of bronchial asthma and right heart failure
					Exploratory Thoracotomy
1. H. B., M., 53	Carcinoma, left lung, inoperable	Exploratory thoracotomy	No	550 c.c. at operation	Inadequate replacement therapy
2. G. A., M., 61	Carcinoma, stomach, inoperable	Exploratory thoracolaparotomy	No	450 c.c. before operation, 500 c.c. at operation	Inadequate replacement therapy
3. M. L., M., 59	Carcinoma, cardia, inoperable	Exploratory thoracolaparotomy	No	500 c.c. at operation	Inadequate replacement therapy

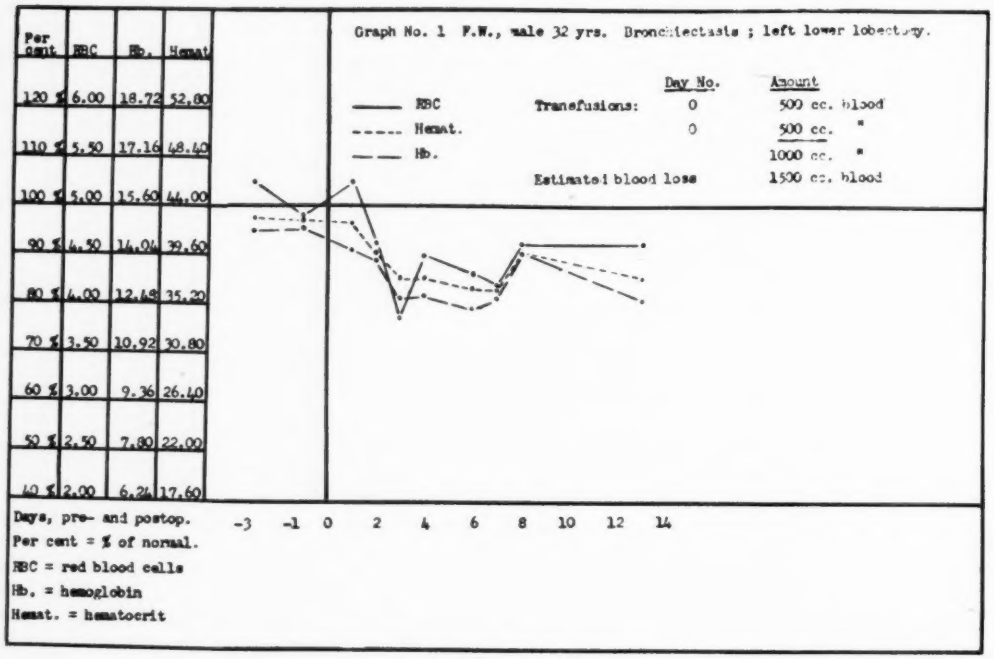
than did the hemoglobin and hematocrit in which 15.6 Gm. per cent and 44 per cent were considered as average normal figures. The figure of 15.6 Gm. per cent as equal to 100 per cent is probably higher than the figure more commonly accepted and were this "normal" lowered the difference would only be accentuated. Also, since three of the exceptions to this statement are women and a more normal figure for them would be 4.5 million red cells, one can even say that in 75 per cent of the patients studied the red cell count reflects a better blood status than does the hemoglobin or hematocrit. Examples of this are seen in Graphs 3, 4, and 5.

—Cont'd

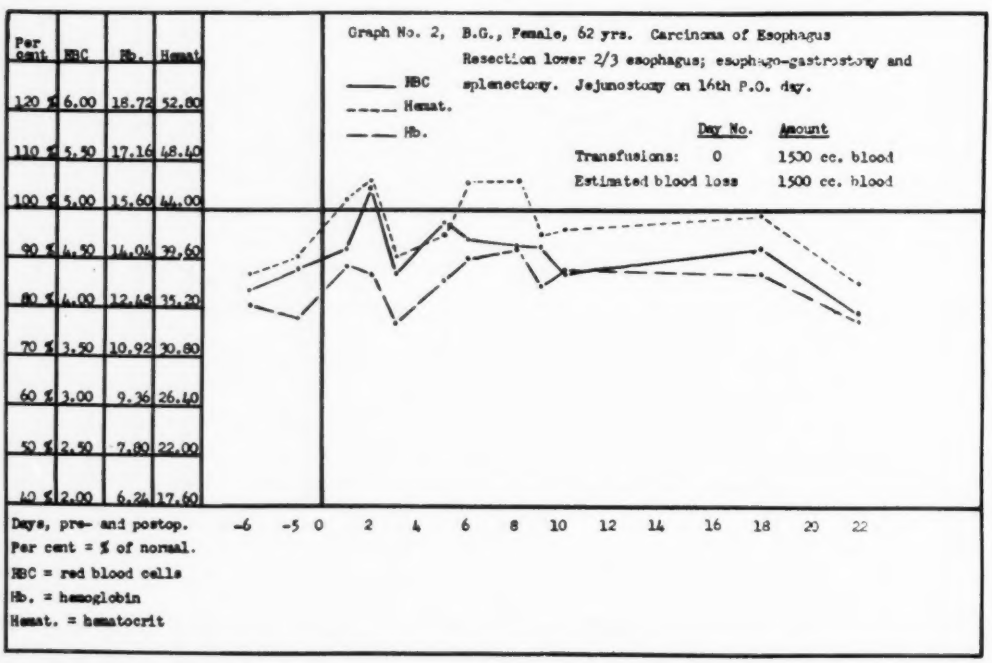
HEMOGLOBIN (GM. %)					HEMATOCRIT (% OF TOTAL BLOOD)					ERYTHROCYTE COUNT (MILLIONS PER CU. MM.)				
PRE-OPERATIVE	FALL	POST-OPERATIVE	DAY FALL	DAY RETURN	PRE-OPERATIVE	FALL	POST-OPERATIVE	DAY FALL	DAY RETURN	PRE-OPERATIVE	FALL	POST-OPERATIVE	DAY FALL	DAY RETURN
(5)														
12.3	.3	12.0	3	13.3 on Day 5	39.9	--	39.9 on Day 3	--	37.3 on Day 22	4.42	.08	4.34	3	3.96 on Day 22
12.8	1.4	11.5	6	11.5 on Day 6	38.2	--	39.1 on Day 4	--	34.7 on Day 6	4.62	--	5.31 on Day 4	--	3.71 on Day 6
13.5	6.4	7.1	3	11.3 on Day 10	39.9	17.4	22.5	3	35.3 on Day 10	5.70	2.87	2.83	3	4.07 on Day 10
13.3	3.1	10.2	10	--	42.2	10.1	32.1	3	--	4.68	.94	3.74	3	4.03 on Day 10
13.3	4.6	8.7	4	10.2 on Day 8	37.9	11.5	26.4	4	32.1 on Day 8	4.37	1.62	2.73	4	3.64 on Day 8
(3)														
10.3	No fall	12.9 on Day 3	--	--	32.6	No fall	40.4 on Day 3	--	--	4.23	No fall	4.92 on Day 3	--	--
13.2	2.6	10.6	11	12.1 on Day 18	40.2	7.9	32.3	1	35.6 on Day 18	4.68	.87	3.81	7	4.03 on Day 18
13.6	1.1	12.5 on Day 1	--	--	40.5	No fall	46.4 on Day 1	--	--	4.52	No fall	4.70 on Day 1	--	--
and Thoracolaparotomy (3)														
12.0	7.0	11.3	11	--	38.8	2.4	36.4	4	37.4 on Day 11	4.60	.13	4.47	1	4.66 on Day 11
13.2	2.4	10.8	3	11.0 on Day 10	38.3	4.4	33.9	3	34.2 on Day 11	4.01	--	4.17	--	4.75 on Day 10
13.2	2.5	10.7	7	--	40.9	7.9	33.0	1	34.7 on Day 7	5.62	1.39	4.23	7	

One patient, M. W. (see Graph 6), showed the greatest postoperative fall in hemoglobin, hematocrit, and erythrocyte count, respectively, a fall of 6.4 Gm. per cent, 17.4 per cent, and 2.87 million, so that on the third postoperative day the patient's blood status was 7.1 Gm. per cent of hemoglobin, 22.5 per cent hematocrit, and 2.83 million red cell count, and it must be emphasized that the cause of this severe drop was hemorrhage into the operative wound. The three patients undergoing exploratory thoracotomy were given an average of 500 c.c. whole blood at operation and, although in the absence of extensive resection blood loss is not so great as in some of the other operations listed,

the surgeon felt that each of these had had inadequate replacement to restore the blood to a normal status. The two patients with transthoracic vagotomy received no blood at operation. However, no greater change of blood status was observed in these two patients than in others and it must be concluded

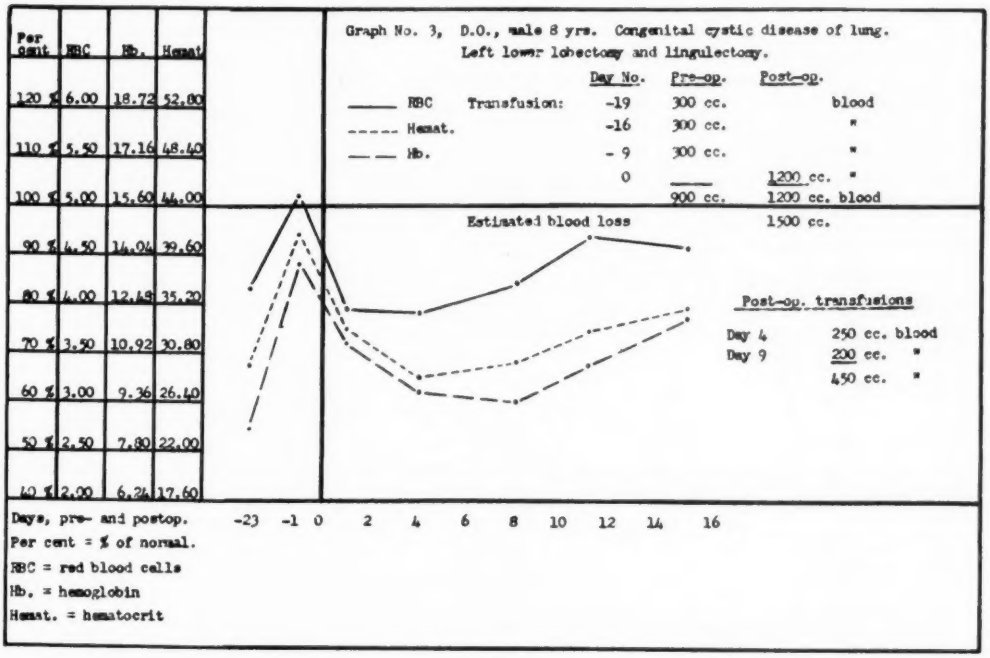

Graph No. 1 F.W., male 32 yrs. Bronchiectasis ; left lower lobectomy.
RBC
Hemat.
Hb.
Transfusions:
Day No. Amount
0 500 cc. blood
0 500 cc. "
1000 cc. "
Estimated blood loss 1500 cc. blood
Per cent RBC Hb. Hemat.
120 % 6.00 18.72 52.80
110 % 5.50 17.16 48.40
100 % 5.00 15.60 44.00
90 % 4.50 14.04 39.60
80 % 4.00 12.48 35.20
70 % 3.50 10.92 30.80
60 % 3.00 9.36 26.40
50 % 2.50 7.80 22.00
40 % 2.00 6.24 17.60
Days, pre- and postop. -3 -1 0 2 4 6 8 10 12 14
Per cent = % of normal.
RBC = red blood cells
Hb. = hemoglobin
Hemat. = hematocrit

Graph 1.

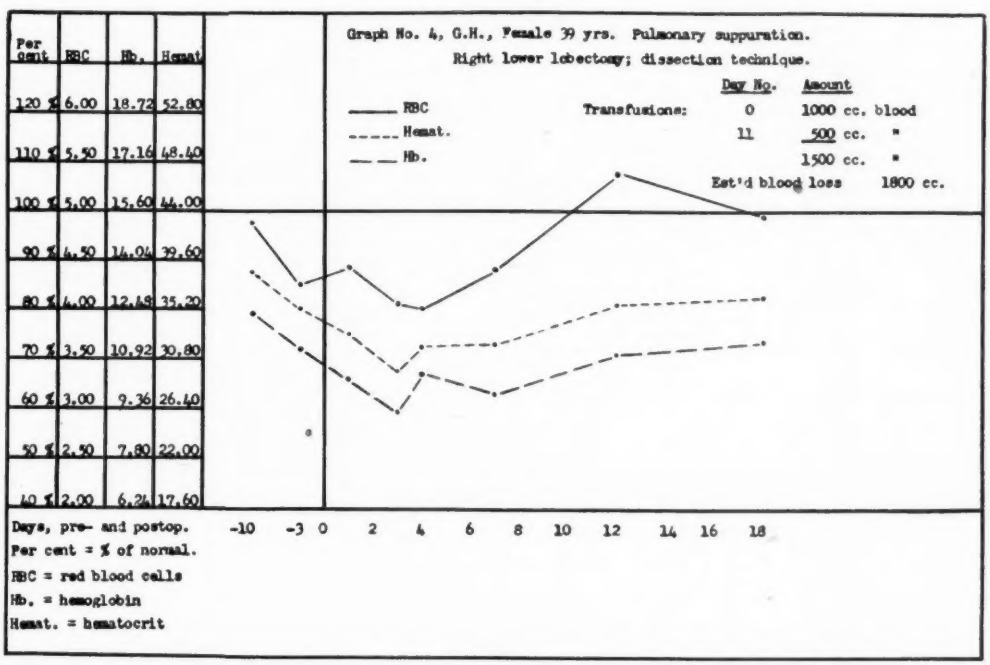

Graph No. 2, B.G., Female, 62 yrs. Carcinoma of Esophagus
Resection lower 2/3 esophagus; esophago-gastrostomy and splenectomy. Jejunostomy on 16th P.O. day.
RBC
Hemat.
Hb.
Day No. Amount
Transfusions: 0 1500 cc. blood
Estimated blood loss 1500 cc. blood
Per cent RBC Hb. Hemat.
120 % 6.00 18.72 52.80
110 % 5.50 17.16 48.40
100 % 5.00 15.60 44.00
90 % 4.50 14.04 39.60
80 % 4.00 12.48 35.20
70 % 3.50 10.92 30.80
60 % 3.00 9.36 26.40
50 % 2.50 7.80 22.00
40 % 2.00 6.24 17.60
Days, pre- and postop. -6 -5 0 2 4 6 8 10 12 14 16 18 20 22
Per cent = % of normal.
RBC = red blood cells
Hb. = hemoglobin
Hemat. = hematocrit

Graph 2.

that these patients were no more seriously undertreated as far as replacement therapy is concerned than were other patients who had more extensive operations and larger transfusions.

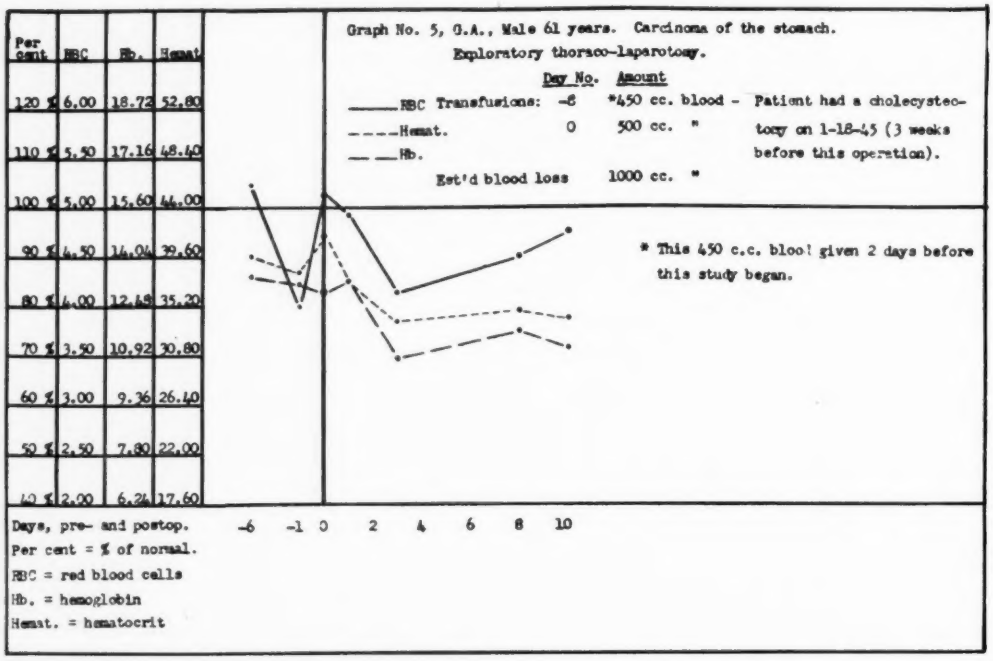

Per cent
RBC
Hb.
Hemat
120 % 6.00 18.72 52.80
110 % 5.50 17.16 48.40
100 % 5.00 15.60 44.00
90 % 4.50 14.04 39.60
80 % 4.00 12.48 35.20
70 % 3.50 10.92 30.80
60 % 3.00 9.36 26.40
50 % 2.50 7.80 22.00
40 % 2.00 6.24 17.60
Graph No. 3, D.O., male 8 yrs. Congenital cystic disease of lung.
Left lower lobectomy and lingulectomy.
Day No. Pre-op. Post-op.
RBC Transfusion: -19 300 cc. blood
Hemat. -16 300 cc. "
Hb. - 9 300 cc. "
0 ____ 1200 cc. "
900 cc. 1200 cc. blood
Estimated blood loss 1500 cc.
Post-op. transfusions
Day 4 250 cc. blood
Day 9 200 cc. "
450 cc. "
-2½ -1 0 2 4 6 8 10 12 14 16
Days, pre- and postop.
Per cent = % of normal.
RBC = red blood cells
Hb. = hemoglobin
Hemat. = hematocrit

Graph 3.

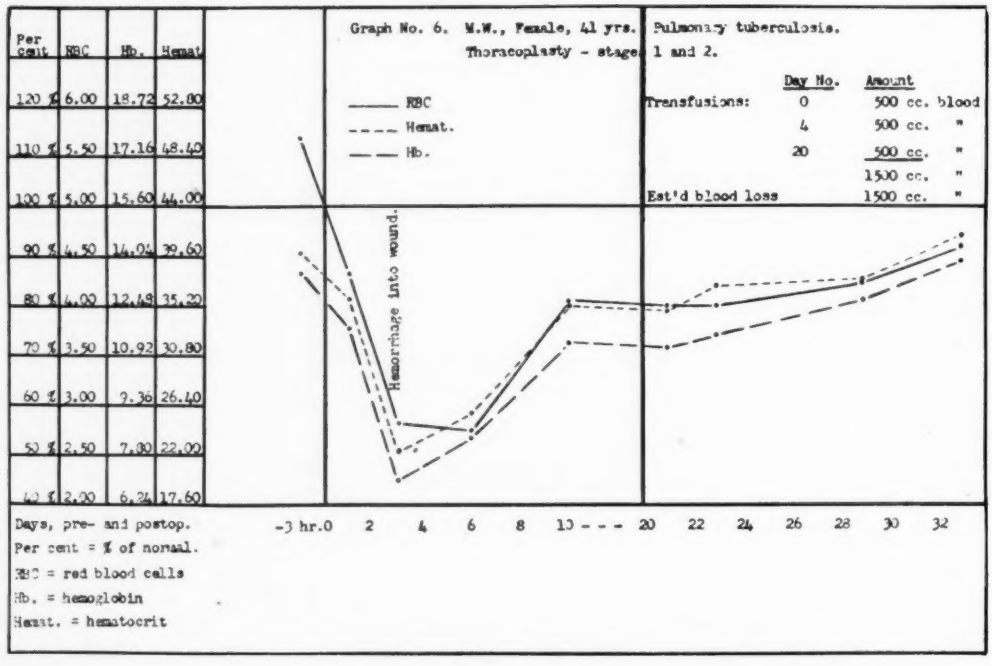

Per cent
RBC
Hb.
Hemat
120 % 6.00 18.72 52.80
110 % 5.50 17.16 48.40
100 % 5.00 15.60 44.00
90 % 4.50 14.04 39.60
80 % 4.00 12.48 35.20
70 % 3.50 10.92 30.80
60 % 3.00 9.36 26.40
50 % 2.50 7.80 22.00
40 % 2.00 6.24 17.60
Graph No. 4, G.H., Female 39 yrs. Pulmonary suppuration.
Right lower lobectomy; dissection technique.
Day No. Amount
RBC Transfusions: 0 1000 cc. blood
Hemat. 11 500 cc. "
Hb. 1500 cc. "
Est'd blood loss 1800 cc.
-10 -3 0 2 4 6 8 10 12 14 16 18
Days, pre- and postop.
Per cent = % of normal.
RBC = red blood cells
Hb. = hemoglobin
Hemat. = hematocrit

Graph 4.

In Table III are listed the five patients of this series on whom plasma volumes were determined. The patient's weight is shown and the blood volumes are estimated from body weight according to the method of Schafer,[12]


Per cent
RBC
Hb.
Hemat
120 % 6.00 18.72 52.80
110 % 5.50 17.16 48.40
100 % 5.00 15.60 44.00
90 % 4.50 14.04 39.60
80 % 4.00 12.48 35.20
70 % 3.50 10.92 30.80
60 % 3.00 9.36 26.40
50 % 2.50 7.80 22.00
40 % 2.00 6.24 17.60
Graph No. 5, G.A., Male 61 years. Carcinoma of the stomach.
Exploratory thoraco-laparotomy.
Day No. Amount
RBC Transfusions: -6 *450 cc. blood - Patient had a cholecystectomy on 1-18-45 (3 weeks before this operation).
Hemat. 0 500 cc. "
Hb.
Est'd blood loss 1000 cc. "
* This 450 c.c. blood given 2 days before this study began.
Days, pre- and postop. -6 -1 0 2 4 6 8 10
Per cent = % of normal.
RBC = red blood cells
Hb. = hemoglobin
Hemat. = hematocrit

Graph 5.


Per cent
RBC
Hb.
Hemat
120 % 6.00 18.72 52.80
110 % 5.50 17.16 48.40
100 % 5.00 15.60 44.00
90 % 4.50 14.04 39.60
80 % 4.00 12.48 35.20
70 % 3.50 10.92 30.80
60 % 3.00 9.36 26.40
50 % 2.50 7.80 22.00
40 % 2.00 6.24 17.60
Graph No. 6. M.W., Female, 41 yrs. Pulmonary tuberculosis.
Thoracoplasty - stage 1 and 2.
RBC
Hemat.
Hb.
Day No. Amount
Transfusions: 0 500 cc. blood
4 500 cc. "
20 500 cc. "
1500 cc. "
Est'd blood loss 1500 cc. "
Hemorrhage into wound.
Days, pre- and postop. -3 hr. 0 2 4 6 8 10 - - - 20 22 24 26 28 30 32
Per cent = % of normal.
RBC = red blood cells
Hb. = hemoglobin
Hemat. = hematocrit

Graph 6.

namely, $\frac{2}{25}$ of body weight with a normal hematocrit of 45 per cent. Plasma volume, cell volume, and total volume are listed as determined preoperatively, immediately postoperatively, and again seven to twelve days later. The amount of transfusion at the time of operation is given. The hematocrit is listed as determined at the time of the determination of all the blood volumes. Two blood volumes determined immediately after operation are not included because of technical mistakes. The first three patients have basal volumes within 500 c.c. of the estimated volume. The fourth patient's basal volume is 2,167 c.c. below basal volume. The only explanation for this might be the fact that this patient was dehydrated by forty-eight hours of continuous gastric aspiration before the basal volume was determined. Note that the hematocrit determined at this time was 53.3 per cent, the hemoglobin 17.6 Gm. per cent, and the red cell count 6.4 million as seen in Table II. The fifth patient's basal volume is 880 c.c. below estimated volume and there is no known reason for this difference.

In the second part of Table III are listed the differences between preoperative volumes and postoperative volumes as found in the immediate volume determinations and determinations seven to twelve days later. In the first patient the total volume as determined immediately after operation dropped 1,445 c.c. and with 500 c.c. whole blood transfusion at time of operation added this would mean a total blood loss of 1,945 c.c. This patient had an exploratory thoracolaparotomy with no resection and the surgeon estimated a 1,200 c.c. blood loss. In the third patient the determined loss was 1,349 c.c. and no transfusion was given at operation. The fourth patient showed a loss of only 386 c.c. This was the patient who showed marked hemoconcentration before the operation. Note that ten days later when his third plasma volume was determined there was an increase of 795 c.c. over the first plasma volume determination. However, the red cell volume deficit at ten days was 647 c.c., therefore, the total blood volume increase was only 148 c.c.

By seven to twelve days after operation there was, without exception, an increase in plasma volume over the basal plasma volume. This varied from 291 to 795 c.c. There was a fall in red cell volume ranging from 208 to 914 c.c. by seven to twelve days. Hematocrit fall during this time varied from 3.4 to 17.9 per cent, the latter in the fourth patient, who had shown the marked hemoconcentration before operation.

DISCUSSION

Blood loss and its restoration, especially following major surgery in patients with serious disease, is an exceedingly complex physiologic mechanism involving hemopoiesis, protein and electrolyte metabolism, maintenance of an adequately circulating fluid volume, and the hemostatic forces which the body can muster to minimize as much as possible the slow chronic loss of cells and plasma into large operative wounds. That the loss of bloody serum may be of considerable importance, especially when postoperative aspiration is used, has been shown by Thornton, Adams, and Schafer,[6] who found an average loss of 673.3 c.c. serum in twelve patients on whom lobectomies were done. The

TABLE III. BLOOD VOLUME DETERMINATIONS BEFORE AND

PATIENT AGE AND SEX	DIAGNOSIS	OPERATION	WEIGHT (KG.)	ESTIMATED BLOOD VOLUME (C.C.)	PREOPERATIVE BLOOD VOLUMES		
					PLASMA VOLUME	CELL VOLUME	TOTAL VOLUME
1. G. A., M., 61	Carcinoma of stomach, inoperable	Exploratory thoracolaparotomy	68.5	5,480	3,114	2,033	5,147
2. M. L., M., 59	Carcinoma of cardia, inoperable	Exploratory thoracolaparotomy	67.5	5,400	2,935	2,031	4,966
3. M. S., M., 42	Stomal ulcer, recurrent	Transthoracic vagotomy	66.0	5,280	3,065	2,507	5,572
4. G. P., M., 49	Stomal ulcer, recurrent	Transthoracic vagotomy	75.6	6,048	1,824	2,057	3,881
5. C. F., M., 30	Bilateral bronchiectasis	Left lower lobectomy and lingulectomy	66.2	5,296	2,561	1,855	4,416

Difference Between Preoperative Volumes, Immediate Postoperative Volumes, and Postoperative Volumes 7 to 12 Days

PATIENT	PLASMA VOLUME	CELL VOLUME	TOTAL VOLUME	PLASMA VOLUME	CELL VOLUME	TOTAL VOLUME	HEMATOCRIT (%)
G. A.	−952	−493	−1,445	+291	−208	+ 83	3.4
M. L.	–	–	–	+470	−222	+248	6.2
M. S.	−509	−838	−1,349	+482	−914	−432	14.1
G. P.	+252	−638	− 386	+795	−647	+148	17.9
C. F.	–	–	–	+443	−238	+205	7.5

*Detailed studies of the blood volume before and following intrathoracic operations in five patients. The immediate postoperative studies in the second and fifth patients were incomplete. The increase or decrease in plasma volume, cell volume, and total volume are indicated below. It is apparent that a decrease in all values occurs immediately following operation in spite of the fact that the patients receive from 500 to 1,000 c.c. of whole blood for replacement of blood loss. The studies from seven to twelve days following operation show that this deficit was made up chiefly by plasma from the tissues, the return of cell volume to the preoperative level requiring a considerably longer period of time.

hemoglobin concentration of this serum may be as high as 7 to 8 Gm. per 100 c.c. In order to evaluate these changes and thereby properly treat the patient, the surgeon has at his hand the practical technique of counting red cells, determining hemoglobin and plasma protein concentration, estimating blood loss, and critically judging the patient's clinical response to intravenous treatment before and after operation. Accurately measuring blood loss or determining pre- and postoperative blood volumes is not usually practical.

This study emphasizes that even with seemingly adequate blood replacement the patient's blood does not maintain an even status after major thoracic surgery. The average drop in hemoglobin in grams per cent in these patients was 2.1 Gm. and in most patients this drop had not been restored by the end of two to three weeks following operation. It has already been mentioned that most of these patients showed little or no change in the twenty-four hour period immediately after operation. There seem to be two important factors accounting for this minimal change twenty-four hours postoperatively. First, there is a decreased circulating blood volume with vasoconstriction and vary-

Following Intrathoracic Operations in Five Patients*

Replacement (c.c. blood)	Immediate postoperative blood volumes			Postoperative blood volumes, 7 to 12 days			Hematocrit		
	Plasma volume	Cell volume	Total volume	Plasma volume	Cell volume	Total volume	Preoperative	Immediate postoperative	Postoperative (7-12 days)
500	2,162	1,540	3,702	3,405	1,825	5,230	38.3	41.6	34.9
500	–	–	–	3,405	1,809	5,214	40.9	34.7	34.7
0	2,554	1,669	4,223	3,547	1,593	5,140	44.8	39.5	30.7
0	2,076	1,419	3,495	2,619	1,410	4,029	53.3	40.6	35.4
1,000	–	–	–	3,004	1,617	4,621	42.4	43.1	34.9

ing degrees of hemoconcentration or hemodilution; and, second, there is the immediate effect of transfusions given at operation which for a transitory period tend to hold blood status at its preoperative level. After this, however, the level of oxygen carrying constituents of the blood may show a relative fall during the next five or six days. This is produced by an increase in circulating volume and the gradual loss of cells and plasma continuing to seep into the operative wound. Ebert, Stead, and Gibson[5] in 1941 carefully studied the changes in circulating volume and blood constituents during a period in which 15.5 to 19.7 per cent of the total blood volume was drawn by phlebotomy from six normal, healthy, professional blood donors. They were able to show that plasma volume began to increase immediately after blood loss and that its return was apparently governed by the ability of the body to supply plasma protein to the circulating fluid. In normal healthy individuals, in surgical patients whose plasma protein stores are not markedly decreased due to their disease, or in patients whose preoperative treatment has been effective in restoring protein metabolism to approximately normal, the restoration of total circulating fluid and total circulating protein is often a relatively rapid process. Thus, Ebert, Stead, and Gibson[5] found total circulating blood volume returned approximately to preblood loss levels by seventy-two hours and Thornton, Adams, and Schafer[6] found plasma protein concentration returned to preoperative levels by 9.0 days in patients undergoing major intrathoracic operations and to whom blood transfusions were given when deemed necessary. It is not surprising to find, however, a somewhat different picture when changes in red cell volume and hemoglobin are examined. There are no significant red cell reservoirs in man and restoration of red cell volume and hemoglobin concentration after blood loss lags behind the restoration of plasma protein concentrations and the plasma volume. The

results of our plasma and red cell volume determinations substantiate this view. At the end of seven to twelve days postoperatively, the red cell volume is less than preoperative red cell volumes, this deficit varying from 208 to 914 c.c.

Ebert, Stead, and Gibson[5] found in their study that the lowest hematocrit was obtained within twenty-four hours of phlebotomy. Results in surgical patients differ from their experiments in two ways; first, there is whole blood transfusion at the time of blood loss and, second, there is, postoperatively, continued plasma and red cell loss into the operative site. For these reasons the lowest level reached as far as red cells are concerned may not be until three to seven days after the operation.

In most clinics, including our own, the determination to give pre- or postoperative blood transfusions is most often made on the basis of routine blood examinations, namely, the red cell count and the hemoglobin concentration, qualified, of course, by the clinical state of the patient. Thus, much depends on the accuracy of these determinations and the interpretation of accurate results. It has already been pointed out that a normal hemoglobin concentration, red cell count, or hematocrit twenty-four hours after operation may be entirely misleading as to the course of changes to come in the patient's blood status. Our studies would indicate that such determinations be made at least every other day for one week, or more often if the blood change is greater than expected on any one determination. Graph 6 shows how markedly the blood status can change because of hemorrhage and this was unsuspected until the blood determinations were made.

In our surgical service hematocrit determinations are not routinely done. Red cell counts and hemoglobin estimations are done by students who are in their third year clerkships and these determinations are routinely made every one to two days for about one week after major operations and thereafter as indicated. The red cell count is made in the usual manner and the hemoglobin estimation is done with the Sahli instrument in which acid hematin (in a calibrated tube) is diluted until a color match is obtained with a similar sized brown glass rod.

Wintrobe[14] said ". . . that hemoglobin of the blood is as a general rule determined with less care and by methods which are more inaccurate than those for the determination of any other constituent of the body . . ." and he listed most of the methods for estimating hemoglobin and gave a critical analysis of these various methods. Karr and Clark[15] in 1941 reported a comparison of various hemoglobin methods as performed by technicians and doctors in several hospitals and clinics. They pointed out the well-known sources of error in direct colorimetry such as inaccuracy of the instrument and the variability of the human factor in being able to match accurately red or brown colors. Their results show that at least two Sahli instruments in their clinics were inaccurately calibrated to the extent of 1 Gm. hemoglobin or more. Further, and this is of even more importance, they showed that the physicians erred in hemoglobin estimation to the extent that only 71 per cent of their determinations fell within 1 Gm. of the true hemoglobin concentration. This

error was after corrections for inaccurately calibrated instruments were made. True hemoglobin concentration was determined by the Sheard-Sanford photelometer and Van Slyke O_2 capacity methods. In fact, Evelyn[7] reported an accuracy of plus or minus 2 per cent with the photoelectric colorimeter which, as mentioned earlier, is the method by which hemoglobin concentration was determined in this study.

During the course of this study we have checked at random approximately ten students in twenty-seven hemoglobin estimations with the Sahli instrument and have found results comparable to those of Karr and Clark. Only 41 per cent of the determinations by the students were within 1 Gm. of the true hemoglobin estimation, 66 per cent within 2.0 Gm., and only 88 per cent within 3 Gm. No attempt was made to calibrate the Sahli instruments now in use in our clinic. The average mean deviation by the student was 1.23 Gm. and the greatest deviations were plus 3.04 Gm. and minus 1.20 Gm., a range of 4.24 Gm. or approximately 25 per cent of the normal hemoglobin concentration. No emphasis need be drawn to the uselessness or, in fact, to the dangers of such inaccurate determinations and no list of the factors which are responsible for these errors need be made.

Such errors as have been pointed out for the Sahli hemoglobinometer are not, however, unique to that instrument, as all other instruments of direct colorimetry are more or less likewise inaccurate.

At the present the erythrocyte count enjoys considerable popularity as a means of determining blood status but it is common knowledge that even in the hands of technicians individual counts may vary by as much as 500,000 red cells or roughly 10 per cent of the normal red cell count. The mean deviation in the hands of unskilled students is probably this much or more. Certainly the surgeon who bases his transfusion therapy on such determinations should be acutely aware of the magnitude of the possible error. Of as much or more importance in criticizing the red cell count as a valuable and critical adjunct in the determination of the blood status in patients undergoing major thoracic surgery and large whole blood transfusions is the factor brought out in the earlier discussion of this study, namely, that the red cell count even when carefully done in a uniform manner with similar samples of blood tends to be erratic and, in general, gives a more optimistic picture of the blood status than is warranted by accurate hemoglobin or hematocrit determinations. Our results substantiate those of Dieckmann,[17] who found an error of as much as 13.7 per cent in the results of routine red blood cell counts while the error in hematocrit determinations was only 2.0 per cent.

The hematocrit was determined in this study by the use of Van Allen's[8, 9] capillary tubes and we had little or no technical difficulty with this method. There are, however, two or three important sources of error in the determination of the hematocrit and unless these are avoided the hematocrit determination can be as valueless, as has been pointed out, as is the erythrocyte count or the hemoglobin estimation by the more common methods. One of the chief errors in this regard is the improper choice of anticoagulant. It is

well known that the sodium and potassium oxalate salts often used as anticoagulants may change the red cell size by as much as 4 or 5 per cent. Accurate correction for this effect is difficult and may be one of the reasons why the hematocrit has gained as slowly in favor as it has. This difficulty is, however, easily solved by using minute amounts of heparin, which was suggested as an anticoagulant for the hematocrit determination by Mason[16] as long ago as 1924. We have not experimentally compared the various micro- and macro-sized instruments for the hematocrit determination, but from the literature it seems apparent that with sufficient centrifugalization all the methods are quite comparably accurate so long as consideration is given to the anticoagulant. Realizing that it has not been practical to make routine use of the photoelectric colorimeter for hemoglobin determination, we must therefore conclude that of the commonly used techniques the hematocrit determination is the most valuable aid to the surgeon in determining pre- and postoperative blood status. In patients undergoing major thoracic surgery and treated with relatively large whole blood transfusions the greatest changes in blood status occur from the second to the fifth days. During this period the blood picture should be most carefully followed.

SUMMARY AND CONCLUSIONS

The changes in red cell count, hemoglobin estimation, and hematocrit were followed pre- and postoperatively in patients undergoing major thoracic surgery. It was found that even with blood transfusion aimed at replacing the estimated amount of blood lost at operation, values for all of these determinations dropped by as much as 10 to 15 per cent after the operation. The greatest amount of this fall occurred during the second to fifth days after operation.

The changes in hemoglobin estimation and hematocrit were found to parallel each other closely, but the red cell count was erratic and, in general, gave a more optimistic picture of the blood status than was warranted by the hematocrit or hemoglobin estimation. Of these latter two routine methods of determining blood status, the hematocrit is the most valuable both in terms of the technical ease of obtaining accurate determinations and its reliability in following changes in blood status, since gross errors in hemoglobin estimation are obtained with direct colorimetry methods.

In a series of five patients, blood volumes were determined before and after operation. In all, the blood volume was decreased immediately after operation. In every case, with one exception, the total blood volume had returned to its preoperative level by seven to twelve days after operation. This return to preoperative level was due to an increase in plasma volume over and above the preoperative plasma level. The total cell volume showed a deficit varying from 208 to 914 c.c. at seven to twelve days after operation.

It was observed in this study of patients, who for the most part were suffering from chronic lung diseases, that few of them had anemia. Such an observation has been made before in similarly diseased patients and this is

apparently explained by the well-known fact that interference with the oxygen transport function of the lung results in compensatory changes in the blood status.

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EXPERIMENTAL APPENDICAL PERITONITIS

I. The Prognostic Significance of Certain Hematologic Factors, Especially the Prothrombin Time

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INTRODUCTION

THE mechanism of death in appendical peritonitis has been generally assumed to be related to the consequences of the growth within the peritoneal cavity of a variety of intestinal bacteria, chiefly *Escherichia coli,* intestinal streptococci, and Clostridia, with liberation of toxins capable of producing not only local injury, but systemic lesions as well. During the period since the introduction of new chemotherapeutic agents there has been observed a definite reduction in mortality from this disease, but considerable uncertainty has remained as to whether the apparent reduction is due to chemotherapy or to improvement in ancillary methods of treatment, such as maintenance of requirements of fluid, electrolyte and blood, and intestinal decompression. It has been well recognized that the bacteria most frequently found in appendical peritonitis are comparatively insusceptible to the effects of sulfonamides and, to an even greater degree, of penicillin. Therefore, the recent report of Fauley, Duggan, Stormont, anod Pfeiffer,[1] suggesting marked benefit from penicillin in experimental appendical peritonitis in the dog, now confirmed by Ravdin and Frank,[2] made it desirable to attempt to define more precisely the basis of chemotherapy in peritonitis. Because of the importance of peritonitis as a cause of death in penetrating wounds of the abdomen, it was decided that this was a problem of sufficient wartime importance to justify an immediate investigation. It was hoped that advantage might be taken of new advances in our understanding of the basis for the morbid changes in other related diseases such as traumatic shock and burns.

Fauley and his colleagues reported a mortality of 92.6 per cent in control animals in which peritonitis was produced by ligation and subsequent necrosis of the appendix. There was no mortality from peritonitis in animals in which penicillin treatment was commenced immediately after application to the appendix of the peritonitis-inciting ligature, providing animals dying of internal fecal fistula were excluded. The corresponding figures obtained by Ravdin and Frank were 90 per cent and 30 per cent, respectively. In both series, there seemed to be little doubt as to the protective action of penicillin. However, the protective effect of penicillin in peritonitis has not been related

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exclusively to a direct bactericidal or bacteriostatic action of the drug. That other mechanisms may be involved in the protective action of penicillin has been clearly demonstrated by Boor and Miller.[3]

The plan of our investigation was to produce peritonitis in dogs by the same technique used by Fauley and associates, and then to carry out on the animals a variety of biochemical and physiologic measurements in the hope of finding some critical variation between dying and surviving animals which might logically be influenced directly by specific treatment with penicillin or other agents. The work of several previous investigators had provided some useful guides in planning the scope of the study and selecting the techniques to be employed in arriving at the desired goal.

Studies carried out by Bower and his colleagues[4, 5, 6] led to the conclusion that the toxins of *Clostridium welchii* were largely responsible for the lethality of peritonitis. He claimed that plasma from a recovering animal would not only protect another animal from the disease, but would also protect the pigeon against *Cl. welchii* toxin. The occurence of *Cl. welchii* in the peritoneal exudates of patients in his clinical series was substantially higher than that reported by other observers. If the interpretation by Bower and associates is correct, the action of penicillin might be accounted for on the basis of a drug-induced inhibition of the activity of *Cl. welchii.*

Meleney, Harvey, and Jern,[7] after a study of 106 cases of peritonitis, concluded that *Esch. coli* and streptococci were of equal or greater importance than *Cl. welchii* in the lesions of peritonitis, and showed that the latter organism was frequently absent from lesions in fatal cases. These and other authors have emphasized the importance of bacterial synergism in peritonitis. However, assigning to any or all of these bacteria the lethal role in peritonitis still leaves the picture incomplete. It remains important to obtain an understanding of the physiologic and biochemical abnormalities which, although perhaps induced by bacterial toxins, are in the last analysis responsible for morbidity and death.

Evidence that disturbances in hemodynamic equilibrium are of importance in peritonitis can be found in reports of Elman[8] and of Scudder and co-workers,[9, 10] based largely on laboratory studies in patients. Elman reported on the successful use of plasma in cases of peritonitis on the basis that peritonitis is associated with marked reduction in circulating blood volume. In attempting to maintain globulin and albumin at normal levels throughout the course of the disease he used as much as 1,000 c.c. of plasma per day, with apparently favorable results. Scudder suggested that the success of therapy in peritonitis (and in some other surgical diseases) could be related to the adequacy with which hydration, electrolyte balance, and protein levels were maintained, and that the use of frequent measurement of the specific gravity of whole blood and of plasma is distinctly helpful as a guide in replacement therapy. This study indicated that the disease is associated with physical changes in blood which were interpreted as representing dehydration and hypoproteinemia, and that correction of these factors results in clinical im-

provement. There can be no doubt that peritonitis results in the loss into the bowel and into the free peritoneal cavity of considerable amounts of water, protein, and electrolytes, with a concomitant reduction in blood volume.

The observations of Altemeier and Jones[11] and of Bisgard and associates[12] concerning the influence of prophylactic x-ray treatment on the resistance of animals and patients to peritonitis seemed possibly relevant to our study. It does not appear that any adequate explanation has ever been advanced for the apparent protective effect of roentgen irradiation of the abdomen, particularly for the presence of a protective antitoxic factor as identified by Bisgard in the circulating plasma of animals exposed to small doses of x-rays.

The foregoing paragraphs are not offered as a review of the voluminous literature on peritonitis, but only to illustrate the variety of approaches which were suggested to us in getting at our principal primary objectives—a further understanding of the basis for the morbid sequences of peritonitis and of the possible role of chemotherapeutic agents in influencing the course of the disease.

This initial paper deals with exploratory studies, during which various hypotheses concerning the morbid process were put to test in an attempt to find one or more factors which might correlate to a statistically significant degree with the mortality from the experimentally produced disease.

MATERIALS AND METHODS

The animals used in this experiment were stray adult dogs obtained through regular channels. They varied in weight from 5 to 15 kg., but averaged about 9 kg. The animals were "debarked" under nembutal anesthesia on the day of arrival and then kept under observation until such time as they were to be used, but always for a period of at least two weeks. The dogs were maintained in clean cages on a diet of "Munchy" dog meal,* supplemented with fresh meat twice weekly whenever such was available. The original fifteen dogs were animals which had been in our colony for one year or more and on which other experimental procedures had been carried out, none of them involving laparotomy or injury to the peritoneum.

Technique of Production of Peritonitis.—Intravenous nembutal anesthesia, 30.0 mg. per kilogram in 5 per cent solution, was used. The abdomen was opened through a right lateral rectus incision and the appendix identified. The mesoappendix was dissected free and the vessels ligated with silk. An obstetrical tape tie was then applied tightly about the base of the appendix, care being taken not to break the continuity of the bowel. A culture was obtained from the cecum by aspirating some feces through a 16 gauge needle into a syringe. The needle hole was closed with a silk purse-string suture. The abdominal wall was closed in three layers, using a continuous silk suture on the peritoneum and interrupted silk sutures on fascia and skin. A collodion dressing was applied to the operative wound.

*Manufactured by Parke and Pollard, Boston, Mass.

Postoperative Treatment.—Immediately postoperatively 50.0 c.c. of castor oil were placed in the animal's stomach through a stomach tube, after the technique of Fauley and associates. Bower had suggested that this procedure increased the mortality rate in experimental peritonitis.

Postoperatively most of the animals were given 20.0 c.c. per kilogram of 2.5 per cent glucose and 0.5 per cent normal saline solution intravenously every twelve hours. A small group of animals was given water by mouth ad libitum and another small group was given 20.0 c.c. per kilogram of water by mouth every twelve hours.

Animals subjected to this experimental procedure had a rather typical postoperative clinical course. Each animal's condition was observed at twelve-hour intervals postoperatively, and at these time intervals blood was drawn for the physical and biochemical determinations. On the basis of "clinical" observations, the following stages in the disease were noted and named: Stage I, The Preoperative Phase; Stage II, the Postoperative Crisis; Stage III, Recovery from Postoperative Crisis; Stage IV, the Crisis of Peritonitis; and, if the animal survived, Stage V, Recovery. Stages II, III, and IV varied in duration between animals.

The Postoperative Crisis was characterized by a rise in temperature and respiratory rate, the animal being prostrate in the cage. The respirations were deep and full and cyanosis was never seen during this period. This was the typical condition of the dog at the twelve-hour postoperative period.

By twenty-four hours, the animals seemed usually to have recovered from the immediate effects of the operation and would, as a rule, respond to attention by standing up. The temperature readings varied slightly, but in the majority of cases temperatures of normal or near normal levels were recorded. The respirations invariably returned to normal during this stage, the Recovery From the Postoperative Crisis.

This period of relative improvement lasted twelve to forty-eight hours. Following this the clinical condition of the animal changed markedly with the onset of the Crisis of Peritonitis. The temperature and respirations rose, abdominal rigidity was noted, and the animal again was unable to rise. The respirations at this time were often very shallow, cyanosis was frequently seen, and the peripheral veins were dilated and dark in color so that they stood out clearly against the background of surrounding shaved skin. Stage IV lasted for from twelve to forty-eight hours.

Recovering animals (Stage V) showed a return of all factors to normal, and this recovery usually occurred rather abruptly, within a twelve-hour period, so that recovery seemed to be by crisis rather than by lysis, although many of the animals remained in weakened condition for a few days.

Autopsies.—In a few preliminary experiments animals were sacrificed on the second, third, and fourth days in order to ascertain the course of local changes. By the second day the appendix had become a necrotic sack which had usually not ruptured, but evidence of generalized peritoneal infection could be discerned. By the third day there existed a diffuse peritonitis with

a completely gangrenous ruptured appendix. It seemed probable that rupture of the necrotic fluid-filled sac sometimes occurred rather suddenly, flooding the peritoneal cavity with as much as 100.0 c.c. of fluid, containing many bacteria and their toxins and products of tissue and bacterial decomposition. The further sequences might be influenced to some degree by whether this leakage was abrupt or gradual. On the fourth day the omentum had begun to envelop the area of maximal necrosis, although abdominal exudate remained thick and malodorous.

Animals which died were autopsied within six hours; all other animals were autopsied on the tenth postoperative day. By this time a localized abscess of varying size was always present, acute inflammation of other peritoneal surfaces had subsided, but considerable amounts of clear or slightly turbid fluid were occasionally found. Cultures of the abdomen always yielded a variety of intestinal organisms. Autopsies done on animals dying during the first seventy-two hours confirmed the preliminary findings, except that the tendency for localization of the abscess was rarely seen, the bowel showed many serosal hemorrhages, and the abdominal exudate was grossly hemorrhagic.

In addition, extensive lesions of the lungs were regularly noted on gross examination. (The trachea was ligated before the thorax was opened.) There frequently existed a frank pneumonia, but in many cases the picture was indicative of atelectasis with vascular engorgement and parenchymal hemorrhage. Microscopic studies confirmed these findings and also revealed that the vascular engorgement was by no means confined to the lungs. Sections of liver, kidney, spleen, and adrenal showed dilated vessels and capillaries filled with red blood cells with occasional hemorrhages into the parenchyma of each of these organs.

Experimental Methods.—

Collection of blood: Blood was taken under sterile precautions from the jugular veins of the animals every twelve hours, beginning preoperatively, and until the seventy-second postoperative hour. For biochemical studies, the blood was taken under oil and without an anticoagulant. The clotted specimen was centrifuged and the serum removed for study.

Blood for physical studies was taken in a dry syringe and immediately placed in small bottles containing 0.006 Gm. of ammonium oxalate and 0.004 Gm. of potassium oxalate per 5.0 c.c. of blood.

Laboratory Methods.—Nonprotein nitrogen was determined by the micro-Kjeldahl technique. Protein determinations were done after the method of Barbour and Hamilton as modified by Weech, Reeves, and Goettsch[13] and, in some cases, by the copper sulfate method of Phillips and Van Slyke.[14] Chloride determinations were done by the Volland titration. Sodium and potassium determinations were carried out on the flame photometer.* Calcium levels were measured by the technique of Collip and Clark. Oxyhemoglobin was measured with the Evelyn photocolorimeter.

*These determinations were done with the cooperation of the biochemistry laboratory of the Department of Internal Medicine.

Whole blood specific gravity and plasma specific gravity were estimated by the falling drop method, using copper sulfate solutions of varying specific gravity.[14]

Erythrocyte sedimentation rate: Erythrocyte sedimentation rate was measured in a Wintrobe tube and the amount of sedimentation occurring in thirty minutes was read as the end point.

Hematocrit: The level of packed red blood cells in the Wintrobe tube was determined after centrifuging at about 3,000 r.p.m. until no further change occurred.

Prothrombin times: Both whole blood prothrombin times after the method of Abbott (using Abbott's thromboplastin)[15] and plasma prothrombin times by the method of Quick[16] were used. Since the tests gave comparable readings in relation to their respective controls over a long series of experiments, the two tests are not differentiated in the discussions of prothrombin times in this paper.

Red blood cell fragility determinations: Red blood cell fragility determinations were done by the quantitative photoelectric method, described by Hunter.[17]

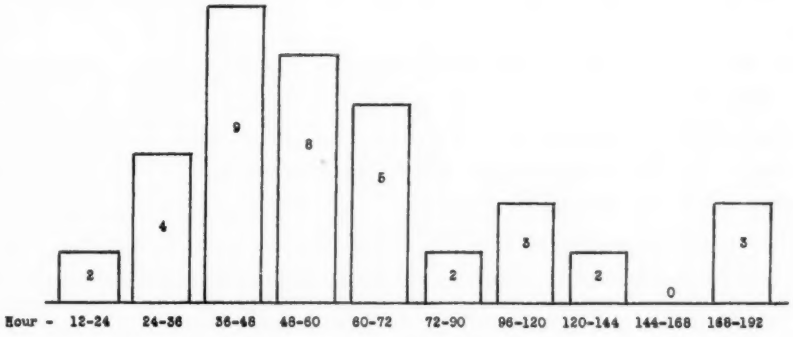

Fig. 1.—Distribution in mortality in experimental peritonitis, incidence of deaths at stated postoperative hours.

EXPERIMENTAL RESULTS

Peritonitis was produced in ninety-one control animals; of these, fifty-three survived and thirty-eight died, a mortality of 41.7 per cent. The time of death varied from 12 to 192 hours postoperatively, the majority of deaths occurring at between twenty-four and seventy-two hours (Fig. 1).

In order to determine the possible effect of allowing the animals to have fluid ad libitum, a group of twenty-four animals were subjected to the experimental procedure and no attempt made to restrict fluids postoperatively, water being offered freely. Of this group twelve animals had been in the colony for one year or more and twelve animals were of the group obtained specifically for this experiment and referred to as "new colony" dogs.

In Table I are shown the mortality statistics in this group, compared with the remainder of the control dogs who received only 20.0 c.c. of fluid per kilogram every twelve hours. Although at first glance it may seem that the method of fluid administration is accountable for the difference, a closer analy-

TABLE I

DOGS	WATER AD LIBITUM		SALINE-GLUCOSE (40 C.C. PER KILOGRAM PER DAY)	
	LIVED	DIED	LIVED	DIED
"Old" colony	11	1	3	0
"New" colony	7	5	32	32
Total	18	6	35	32

sis reveals that the figures are significant only in respect to the previous history of the animal in the colony.

These results suggest that the dogs which were in the colony for a long time were more resistant to this experimental disease. The reason for this was not immediately apparent, although diet and previous experimental procedures were considered, as well as a possible measure of acclimatization against pulmonary infection in the "old" colony dogs.

A number of biochemical studies were carried out in somewhat random fashion in an attempt to determine what measurements might correlate sufficiently well with death or survival to justify their systematic use in subsequent studies.

Nonprotein nitrogen levels were followed throughout the course of the disease in fifteen animals. Of these, nine lived and six died. In the surviving group the highest reading was 75.0 mg. per 100 c.c. the lowest 26.0, and the mean 36.0. In the dying group the highesf value was 71.0 mg. per 100 c.c., the lowest 23.0 and the mean 46.0.

Total protein concentrations showed a fall on the third postoperative day in the surviving animals, coincident with hemodilution. During the acute stage of the disease, however, there was no significant difference between the values in the surviving and dying animals. Falling-drop protein tests (Barbour and Hamilton) were done on fifteen dogs while plasma specific gravities and protein calculations by the copper sulfate method were done on the remaining seventy-six. The range of protein values during the crisis of peritonitis was, in the surviving animals (in grams per 100.0 c.c.), high 7.7, low 5.0, and mean 5.4; in the dying animals, high 7.5, low 5.0, and mean 5.55. There was no correlation between the preoperative values (which ranged from 4.8 to 6.9 Gm. per cent of protein) and the subsequent course of the disease.

Chloride determinations were done on animals which received intravenous fluids as well as on those which took fluids by mouth. Although the chlorides were maintained at a higher level in the first group, there was again no correlation between the chloride level and the outcome of the final crisis.

Sodium and potassium levels were followed on only four animals, two of which lived and two of which died. Slight variations occurred during the course of the disease but there was no significant difference between the two pairs. In the two animals that died the last determination made shortly before death showed sodium levels of 141 and 139 m.eq./L and potassium levels of 4.7 and 3.9 m.eq./L. The surviving animals showed during the crisis of peritonitis

sodium levels of 137.0 and 139.0 meq. per liter and potassium levels of 4.7 and 3.5 meq. per liter.

The results of bacteriologic examinations are shown in Table II. There is no correlation between the types of organisms involved and the mortality. It is true that pathogenic organisms were found with greater frequency in cultures from the abscess and peritoneal exudate than in fecal cultures taken at the time of operation, but the pathogens occurred with almost equal frequency in the exudates of animals which survived and of those which succumbed.

TABLE II

TYPE OF ORGANISM	LIVED (TOTAL, 53)		DIED (TOTAL, 38)	
	CECUM CONTENTS	EXUDATE	CECUM CONTENTS	EXUDATE
Esch. coli	47	42	33	34
Enterococci	50	30	33	21
B. welchii	40	37	31	25
Str. viridans	44	37	31	23
B. proteus	16	12	1	16
Beta hemolytic streptococcus	1	23	1	8
Nonhemolytic streptococcus	19	12	10	8
Bacteroides	13	12	6	3
Staph. albus	2	12	1	7
Unidentified gram-negative bacilli	0	2	0	4
Bacillus A	1	5	1	3
Lactobacillus acidophilus	7	1	3	1
Diphtheroids	6	9	7	5
B. alcaligenes	4	3	1	0
Anaerobic streptococcus	3	1	1	1
Unidentified anaerobic gram-positive bacilli	7	11	1	5
B. subtilis	4	3	2	1
B. mucosus capsulatus	2	3	1	0
Hemolytic Staph. aureus	2	3	0	0
Staph. citreus	1	0	0	1
Cl. septique	1	0	0	1
B. pyocyaneus	0	1	0	1
B. chauvoei	0	1	0	0

The biochemical and bacteriologic observations which have so far been reviewed have failed to bring out characteristic differences between surviving and dying animals. However, certain consistent changes in some of the physical characteristics of blood were noted which seemed constantly to correlate with the stage of the disease. An effort has been made in Table III to show this correlation, with data from six representative animals.

Red blood counts, white blood counts, and hemoglobin showed no differences of significance in the dogs surviving and dying, although they followed a typical course, the white blood count rising early and falling slowly, if the animal survived. The red blood count and hemoglobin, after an occasional slight rise at the twelve-hour period, returned to normal for twelve to twenty-four hours and subsequently fell sometimes to strikingly low levels, if the animal survived. This fall in red blood count was frequently associated with serum jaundice, which in one case was clinically evidenced by jaundiced sclerae.

TABLE III. CORRELATION BETWEEN THE COURSE OF EXPERIMENTAL PERITONITIS AND DEVIATIONS OF SELECTED BLOOD FACTORS

	STAGE I	STAGE II	STAGE III	STAGE IV	STAGE V
Rise in H Rise in W.B. Sp. Gr. Decrease in F Prolonged PT time Decrease in ESR 2+		147– H, WB, ESR, PT, F 150– H, WB, ESR, PT *158– H, WB, ESR, PT, F *162– H, WB, ESR, PT, F *164– H, WB, ESR, PT 180– H, WB, ESR, PT		147– H, WB, ESR, PT, F 150– H, WB, ESR, PT *158– H, WB, ESR, PT *162– H, WB, ESR, PT, F *164– H, WB, ESR, PT, F 180– H, WB, ESR, PT	
1+			147– H, WB *158– H, ESR, PT, F *162– ESR, PT *164– PT 180– ESR		
0	147 150 *158 *162 *164 180		147– PT, F 150– PT, H 180– WB		147– PT, F 150– PT 180– PT
1–		*164 (F)	147– ESR 150– WB, ESR *158– WB *162– H, WB, F *164– H, WB, ESR, F 180– WB		147– H, WB, ESR
2–					150– H, WB, ESR 180– H, WB, ESR

*Animal Died.
H, Hematocrit.
WB, W.B. Sp. Gr., Whole blood specific gravity.
ESR, Erythrocyte Sedimentation Rate.
PT, Prothrombin Time.
F, Fibrinogen.

In addition, during Stage IV, the Crisis of Peritonitis, hemolysis was frequently observed, and many of the animals showed a progressive curve of hemolysis, the blood taken every twelve hours showing increasing hemolysis up to the time of the crisis and then decreasing hemolysis and serum jaundice.

The thirty-minute erythrocyte sedimentation rate became markedly reduced during the postoperative crisis. It increased during Stage III, decreased again (frequently to zero) during Stage IV, and when recovery occurred, the rate would invariably be very rapid, frequently reaching 50 to 70 mm. in thirty minutes.

Variations upward and downward in the whole blood specific gravity and the hematocrit tended to follow the same general pattern. A decrease of the thirty-minute erythrocyte sedimentation rate was accompanied by an increase of the whole blood specific gravity and of the hematocrit, and an increase in the thirty-minute erythrocyte sedimentation rate was accompanied by a fall in whole blood specific gravity and hematocrit.

These changes were most marked in the shift from Stage IV to Stage V, Recovery From the Crisis of Peritonitis. Thus, within a period of twelve hours the sedimentation rate might change from 0 to 40 mm. or more, and the whole blood specific gravity might simultaneously fall from 1.060 to 1.050 or less, this change being unassociated with a comparable drop in red cell count or hemoglobin. Recovery From the Crisis of Peritonitis was marked by a fairly precipitate drop in whole blood specific gravity and hematocrit and a concurrent increase in the sedimentation rate. Animals which displayed these changes following a period of critical illness could be said to have passed the danger period.

Since hemolysis had been noted during the crisis of peritonitis, red blood cell fragility tests were made every twelve hours during the course of the disease on a group of seven animals. Changes in fragility appeared concurrently with the previously described changes in specific gravity, hematocrit, and erythrocyte sedimentation rate, the fragility increasing during the postoperative crisis and the crisis of peritonitis, and decreasing during both recovery periods.

Finally, it was observed that the blood taken during the crisis of peritonitis did not clot readily, and when it did clot, it was in the nature of a soft thrombus, and clot retraction did not occur. A preliminary series of whole blood prothrombin time determinations were done at the twenty-four, forty-eight, and seventy-two hour postoperative periods. It appeared that animals whose prothrombin times were consistently normal survived, whereas animals whose prothrombin times were prolonged as much as two or three seconds at the twenty-four and forty-eight hour periods tended to die. An occasional animal in the latter category survived, but remained in poor condition until the prothrombin time had returned to normal.

There appeared to be a relationship between prolongation of prothrombin time and the severity of respiratory distress. Therefore, x-ray examinations of the lungs were performed on a few sick animals. Roentgenograms were taken daily for four days, commencing preoperatively. The results indicated a

definite association between the onset of pulmonary disease and the development of prolongation in prothrombin time. Figs. 2 and 3 show sets of roentgenograms on two representative animals. The first had a normal prothrombin time at the twenty-four, forty-eight, and seventy-two hour periods, and x-ray

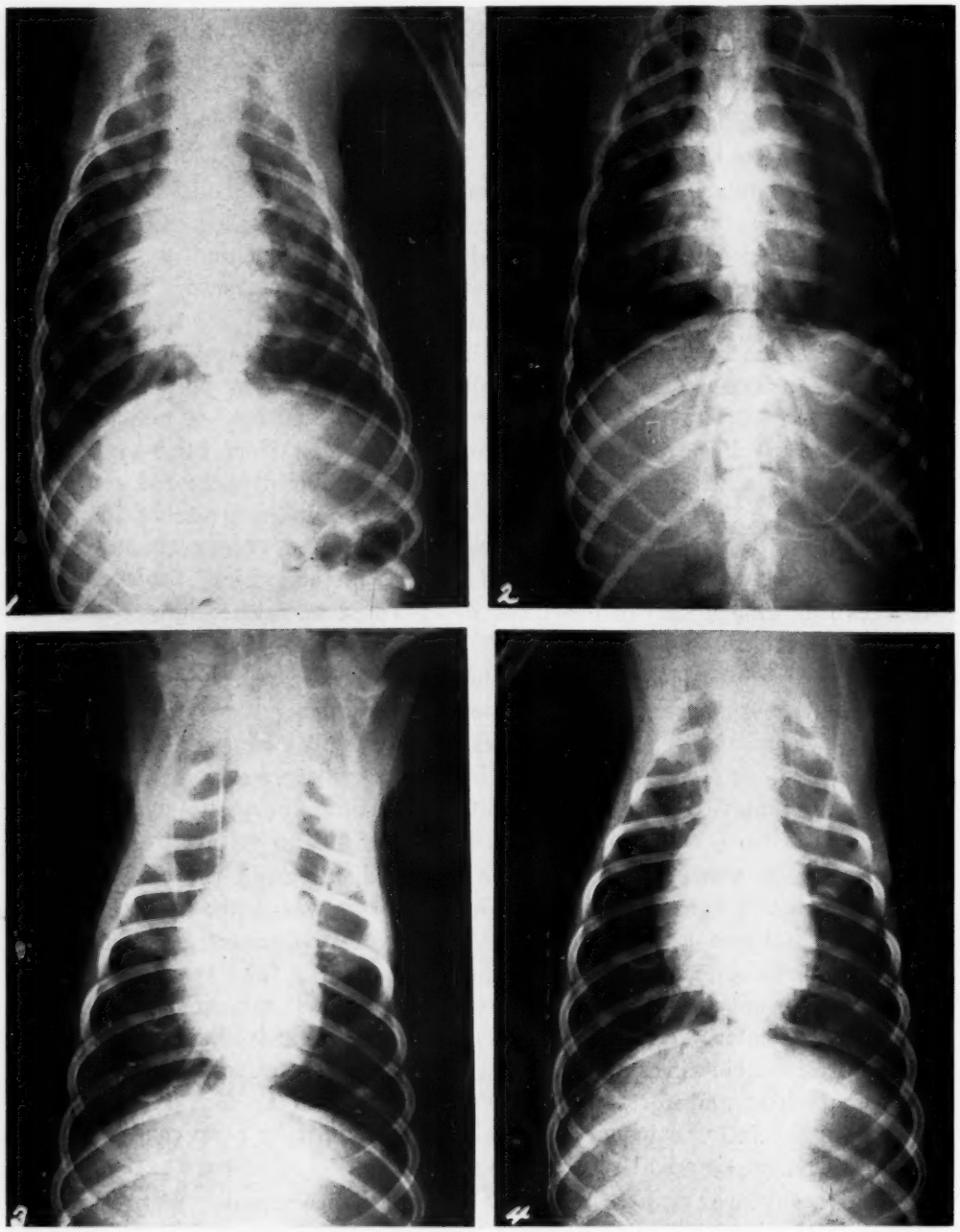

Fig. 2 (Dog 147).—Roentgenograms of lungs during experimental peritonitis. Dog survived. (*1*) Preoperative, (*2*) twenty-four hours postoperative, (*3*) forty-eight hours postoperative, (*4*) seventy-two hours postoperative. These roentgenograms show no significant changes in an animal whose prothrombin time remained normal and who survived.

views taken at the same period showed little abnormality. The second animal, however, showed a prothrombin time of 10/7 at twenty-four hours and of 12/7 at forty-eight hours; this animal died at about seventy hours and the last x-ray

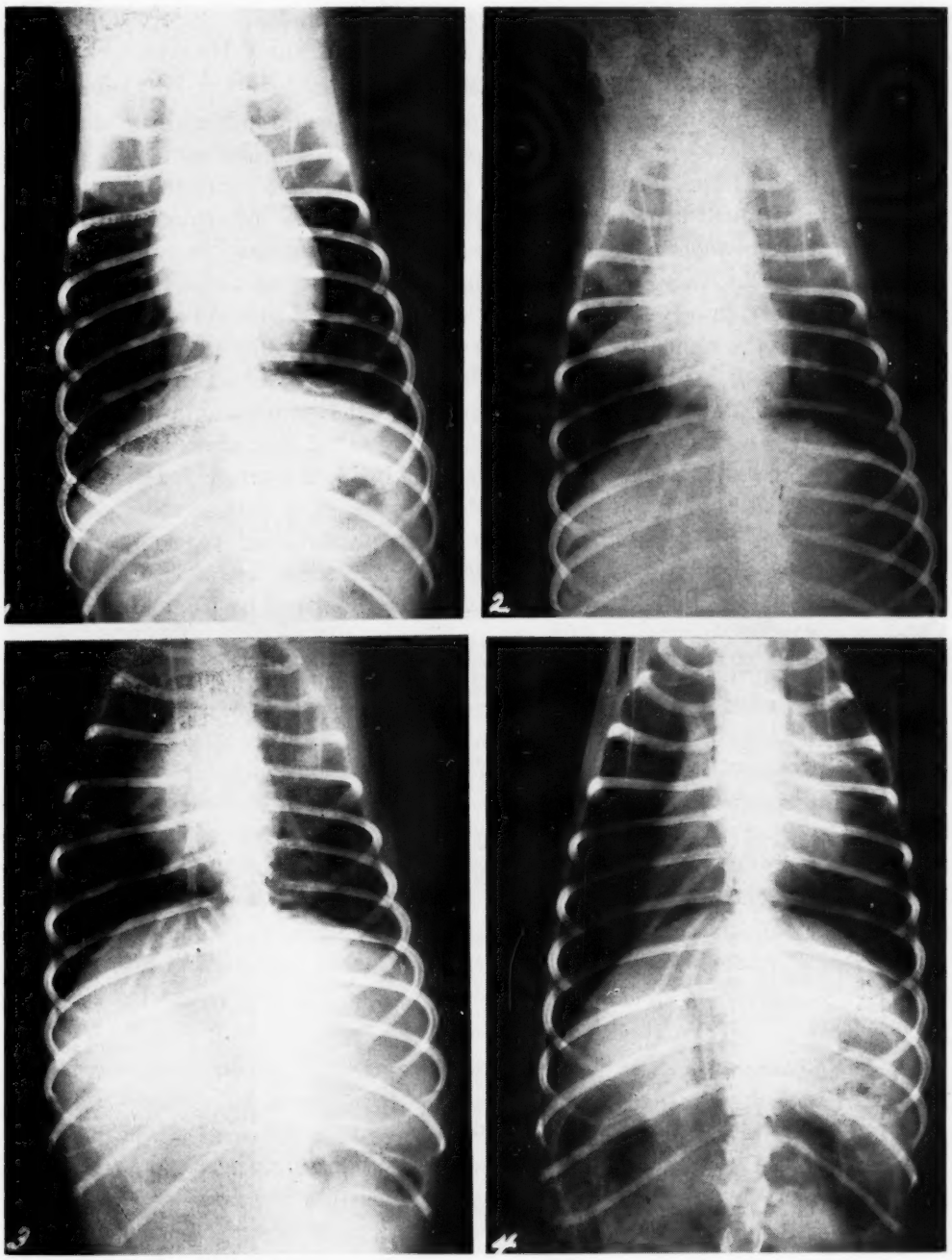

Fig. 3 (Dog 148).—Roentgenograms of lungs during experimental peritonitis. Dog died. (*1*) Preoperative; (*2*) twenty-four hours postoperative, note atelectasis of right middle lobe; (*3*) forty-eight hours postoperative, note disappearance of atelectasis seen in previous view; (*4*) seventy-two hours postoperative (two hours post mortem), note complete atelectasis of right lower lobe. This animal had prolonged prothrombin time throughout the course.

view was taken two hours post mortem. The twenty-four hour roentgenogram showed a type of consolidation consistent with atelectasis, an impression supported by its complete disappearance at forty-eight hours. The post-mortem roentgenogram, before autopsy, showed collapse of the lung and bilateral pneumothorax. Autopsy revealed an early pneumonia in the left upper lobe with bilateral hydropneumothorax, the fluid being frankly bloody in character and showing intestinal organisms on culture.

Because of the apparent significance of the prothrombin time, such estimations were done every twelve hours on all of the animals subsequently studied (Table IV). The changes in prothrombin time correlated with other changes in physical properties of the blood, in that the prothrombin time was consistently prolonged in Stage IV, and returned to normal in Stage V if the animal survived. In general, as had been noted when prothrombin times were done only every twenty-four hours, if the prothrombin time returned to normal in Stage III, the animal tended to survive. If the prothrombin time did not return to normal in Stage III, the animals either died or survived only after severe illness. The prognostic significance of the prothrombin time reading at Stage III is shown in Table V. It should be noted that animals at this stage gave little outward appearance of being acutely ill, the severe reaction to peritoneal infection having not yet commenced.

In view of the possibility that prolonged prothrombin time might be due to increase in circulating heparin, protamine titrations were done on several specimens from each stage, using the technique described by Tagnon.[18]

TABLE IV. WHOLE BLOOD PROTHROMBIN TIMES*

EXPRESSED AS $\frac{\text{PROTHROMBIN TIME OF EXPERIMENTAL ANIMAL}}{\text{PROTHROMBIN TIME OF CONTROL (NORMAL) ANIMAL}}$

DOG NO.	STAGE OF DISEASE				
	I	II	III	IV	V
99	7/7		7/7		7/7
923	7/7		7/7		7/7
119	7/7		13/7	10/7	Died
116	7/7		16/7	Died	
123	7/7		10/7	10/7	Died
141	7/7		7/7	7/7	7/7
137	7/7	14/7		10/7	7/7
138	7/7		7/7	7/7	7/7
144	7/7		12/7	Died	
145	7/7		9/	14/7	7/7†
147	7/7	9/7	7/7	15/7	7/7
148	7/7	10/7	9/7	12/7	Died
149	7/7	7/7	7/7	13/7	7/7
150	7/7	7/7	7/7	10/7	7/7
152	7/7	8/7	8/7	Died	
154	7/7	7/7		9/7	7/7
156	7/7	11/7	14/10	15/7	8/7†
158	7/7	9/7	12/7	13/7	Died
160	10/10	17/7	24/7	38/7	Died
162	8/8	11/8	9/7	12/7	Died
164	5/5	7/5	9/5	10/5	Died
166	7/7	9/7	8/8	8/6	7/7

*Parallel determinations of plasma prothrombin time (Quick) were so similar that these figures have been omitted.

†Survived after extremely stormy course.

TABLE V. PROGNOSTIC SIGNIFICANCE OF PROTHROMBIN TIME BEFORE CRISIS OF PERITONITIS

AT STAGE III	LIVED	DIED	PER CENT MORTALITY
Normal prothrombin time	9	1	10.0
Prolonged prothrombin time	2	10	83.3
Total	11	11	50.0

In no case was the prothrombin time returned to normal by addition of protamine, so it seemed unlikely that heparin was responsible. A sample titration is shown in Table VI.

TABLE VI. PROTAMINE TITRATION (DOG 195)

PROTAMINE CONCENTRATIONS (PER CENT)	PROTHROMBIN TIME (SECONDS)
0.02	30
0.018	28
0.016	24
0.014	19
0.012	19
0.010	19
0.008	19
0.004	19
0.002	19
0.001	19
Control	12

The prolongation in prothrombin time appears to be related to the failure of the clotting mechanism in the blood of animals dying of peritonitis, and to the occurrence of hemorrhagic changes in the peritoneum, liver, and lungs of many of these animals. One obvious explanation of the disturbed clotting mechanism is the development of severe injury to the liver parenchyma from anoxia or bacterial toxins. There seems little doubt but that therapeutic measures capable of giving support to liver function would favor survival if initiated before severe hepatic injury occurs. However, before pursuing this approach to the treatment of peritonitis, it was decided to undertake further investigation of the blood, in order to determine whether all of the morbid hematologic findings described might be traced to a common mechanism. Subsequent studies, which suggest that this mechanism may be a disturbance in the equilibrium between circulating proteolytic and antiproteolytic factors, will be reported in a later paper.

DISCUSSION

Peritonitis resulting from induced gangrene of the dog's appendix is an extremely complex disorder, involving marked disturbances in hemodynamics, significant shifts in water, protein, and electrolyte balance, and functional disturbances of the gastrointestinal tract, the liver, kidney, lungs, and possibly the spleen, adrenals, and hematopoietic system. Any attempt at a determination of what may be the underlying pattern of the morbid sequences is likely to be thwarted by the same obstacles which beset the student of "surgical shock" in any of its forms where differentiation between cause and effect is necessarily difficult. In the study here reported, advantage has been taken of the fact

that about one-half of randomly selected dogs will die when subjected to a uniform experimental procedure and given minimal supportive treatment with water, sodium chloride, and glucose, while the remainder will survive following a stormy illness. Our search has been directed not so much toward characterization of the disease process as a whole as toward detection of what specific differences might exist between the reaction to the disease in surviving animals, as contrasted with animals which died. It is apparent that purely accidental factors beyond experimental control, such as time of perforation of the necrotic appendix, and the effectiveness of omental isolation of the lesion, may play a decisive role in the outcome, although the pathologic findings do not lend support to this interpretation. Of more plausible significance is the role of unknown variables in the previous history and condition of the animals, variables which must always be anticipated among a heterogeneous group of stray dogs. However, it is to no small extent the variable factors in just this poorly defined realm which determine the mortality of peritonitis in man, given similar conditions of surgical management. Differences in bacterial flora may be of some significance, but as in these dogs, the flora of dying and of surviving patients are not qualitatively dissimilar. Fortunately, from the standpoint of the investigator, the disease in dogs builds up to a fairly clear-cut crisis, and upon the reaction to this crisis depends the outcome of the disease. Of all the factors which we have measured, those which have most clearly displayed their lability or reversibility during the crisis of the disease are the whole blood specific gravity, the hematocrit, the erythrocyte sedimentation rate, and the blood-clotting reactions.

Of the greatest specificity has seemed to be the time required for clotting of blood or plasma upon the addition of thromboplastin, the prothrombin time. Animals which best maintained the normality of this reaction throughout the postoperative period were those which tended to survive the crisis of the disease, and those which did not, died.

Therefore, in moving toward a better understanding of the nature of resistance to peritonitis, it would seem desirable to apply to this disease a thorough experimental investigation of fibrinogen, prothrombin, and calcium, and the enzymes and antienzymes, which, taken together, determine the rate, quality, and magnitude of the blood-clotting mechanism.

SUMMARY AND CONCLUSIONS

1. The gross and microscopic autopsy findings in ninety-one animals with induced peritonitis indicate that peritonitis is a systemic disease.

2. The trend toward death or survival in the individual animal cannot be correlated with quantitative changes in nonprotein nitrogen, plasma electrolytes, or total plasma proteins.

3. Systematic study of certain physical properties of blood, notably the hematocrit, erythrocyte sedimentation rate, whole blood specific gravity, and red blood cell fragility, indicates that the disease may be separated roughly into four stages, and that these properties tend to shift simultaneously in the movement of the disease from one stage to another.

4. Changes in prothrombin time not only reflect the various stages of the disease, but also seem to be of prognostic value even before the onset of the disease crisis.

5. Understanding of the morbid processes in peritonitis will be advanced if the basis for abnormalities in the blood clotting mechanism in dying animals can be discerned.

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NEOPLASTIC BILIARY OBSTRUCTION

An Improved Type of Radical Pancreaticoduodenectomy for Ampullary and Pancreatic Cancers

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NEOPLASTIC biliary obstruction was generally a hopeless ailment until the introduction of a successful radical operation by Whipple and his associates[1] in 1935. When those workers showed that the pancreatic duct could be occluded without fatal results in resections of the ampulla of Vater, interest was at once aroused in an attack not only on carcinoma of the ampulla but on cancer of the head of the pancreas as well. The impulse of this discovery was perhaps fortuitous in that later experimental work has shown the advisability of reanastomosis of the pancreatic ducts to the intestine.[2]

Diagnosis.—This presentation is not primarily concerned with diagnostic considerations. About one-third of those cases summarized in this report have histories not of classical painless progressive jaundice, but of jaundice preceded or accompanied by bouts of "biliary pain." The diagnostic studies of Watson[3] and his associates have offered an almost perfect record in this group of cases.

The Development of Radical Pancreatic Duodenectomy.—Prior to 1941, Whipple's original plan of performing pancreaticoduodenectomy in two stages was generally followed. The first was primarily for creation of a new passage by which bile could enter the intestine and thus control the abnormal bleeding tendency associated with biliary obstruction. Usually a gastrojejunostomy was done at this first sitting also to facilitate both preoperative feeding and the performance of the resection of the tumor at a second stage some weeks later.

With the introduction of vitamin K, it became possible to control this bleeding tendency without relief of the biliary obstruction, and, in 1941, Whipple[4] and Trimble and associates[5] independently reported a one-stage operation for the removal of cancers of the head of the pancreas or ampulla of Vater. Aside from the lessened risk of one operation as opposed to two, freedom from the adhesions of a prior stage made complete block resection of these lesions more frequently possible.

Although Whipple and Bauman[6] have shown that patients usually have good fat digestion after exclusion of pancreatic juice from the intestine, some of their patients suffered steatorrhea. Dragstedt[2] noted in animals that a much better nutritive state exists after partial pancreatic resection when a remnant of the pancreas with a duct is left on the duodenum, and suggested implantation of the pancreatic duct into the stomach or intestine as a part of the Whipple pro-

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cedure. Hunt[7] attempted to anastomose the pancreas into the cut end of the severed jejunum in 1941, and a variety of plans for achieving this result have been described by other workers during the past four years.

In line with these findings, the now generally accepted repairs after radical resection of cancer of the head of the pancreas include not only reconstruction of a biliary-intestinal fistula and a gastroenterostomy, but also a pancreaticoenterostomy. The exact types of procedure employed by various authors are of considerable interest, and the most important ones will be briefly sketched later.

Considerations in the Radical Resection.—

Biliary anastomosis: Upon review of the pertinent literature, several considerations become apparent with regard to the performance of a satisfactory operation. The first of these is the prevention of ascending cholangitis following anastomosis between the biliary and intestinal tracts, a complication of considerable frequency in the best of hands. Trautmann, Robbins, and Stewart[8] showed in experimental studies in dogs that simple side-to-side anastomosis of bowel to gall bladder uniformly is followed by passage of intestinal content into the biliary tract. Cole and Reynolds[9] reported the development of suppurative cholangitis in two patients with radical pancreaticoduodenectomy in whom the biliary anastomosis was made distal to the gastric anastomosis. In both, "the chills and fever stopped abruptly when we interrupted the loop of jejunum which had allowed reflux of food into the intrahepatic ducts." We have adopted the plan here of placing the gastric anastomosis well below the biliary one.

Wangensteen[10] made a rather exhaustive study into the literature in connection with the reporting of a case of ascending cholangitis after cholecystjejunostomy; his review of all studies on the subject up to 1928 indicates that the avoidance of stenosis at the site of anastomosis is at least as important as the prevention of reflux from the intestine into the biliary tract.

Pancreatic anastomosis: Another consideration of some importance in the radical resection of the duodenum and the head of the pancreas is that of the handling of the pancreatic duct. In Whipple's first cases and in those of most other authors until 1942, including that previously reported from the University of Minnesota, the pancreatic duct was simply ligated and the cut end of the gland carefully closed with fine silk. The end result of this was usually degeneration of the acinar portion of the remaining pancreas.[2, 6, 11] The experimental work of Whipple and Bauman[4, 6] indicated that most of these patients suffered no serious interference with fat metabolism; this was perhaps due to the leaving of portions of the duodenum containing small accessory pancreatic ducts. In the case reported from here[12] and equivocally in some of those of Brunschwig,[13] instances of steatorrhea were observed, with impaired nutrition. Dragstedt[2] has shown that complete blockage of the pancreatic juice from the intestine of the dog results not only in degeneration of the acini, but interferes with the internal secretion, lipocaic, in one-half the animals, leading to the formation of fatty changes in the livers of these subjects. These findings have led most surgeons to attempt to reanastomose the pancreatic and intestinal lumina in the radical operations.

Simplicity of procedure: A further consideration is the development of the simplest procedure possible, one with a minimum of anastomoses, etc., a factor demanded by the usual poor condition of these patients.

Preoperative preparation: The preoperative preparation of the poor-risk patients must follow the lines that have already been stressed in publications from the department.[14, 15]

Representative Procedures.—

Cancer of the head of the pancreas or of the ampulla with extension into the duodenum, common duct, or pancreas: The original operation of Whipple, Parsons, and Mullens[1] was done in two stages, the first of which was composed of cholecystogastrostomy and gastroenterostomy, and the second of which was resection of the head of the pancreas and much of the duodenum, with inversion of all cut ends (see Fig. 1).

A second type is Whipple's procedure of 1938,[16] in which a wider resection and a Roux Y-plasty permitted him to use the cut end of the jejunum to make an end-to-end anastomosis to the gall bladder.

Hunt[7] (1941) first attempted to anastomose the pancreas to the jejunum in this type of case. An end-to-end pancreaticojejunostomy was made, and the common bile duct was implanted into the side of the bowel. The patient suffered from pancreatic fistulas. Implantation of the common bile duct instead of the gall bladder was adopted by Hunt and others because it had been found that the closed end of the duct was prone to blow out, no matter how carefully closed.

The operation of Trimble, Parsons, and Sherman[5] (1941) introduced the use of the cut end of the stomach directly for the gastrojejunostomy, rather than the more clumsy closure of the end of the stomach and side-to-side gastroenterostomy, as previously.

The operation of Dennis[12] (1942) stressed for the first time the use of a long jejunal loop (40 cm.) between the end-to-end biliary anastomosis and the gastrojejunostomy as a means of preventing reflux of intestinal content into the biliary tract. Gastrointestinal studies on these patients failed at any time to show reflux for more than a fraction of the distance from the stomach to the gall bladder. Likelihood of ascending cholangitis was further reduced by use of the end-to-end cholecystojejunostomy, adopted because it was thought to minimize the likelihood of stenosis. This operation was designed to be as simple as possible; whereas all previous operations had involved a minimum of four suture lines, and several as many as six, this required but three. Trouble was encountered with blowout of the common duct closure, a factor which has led us to employ the common duct directly for anastomosis to the jejunum.

Whipple's operation of 1943[17] incorporates this general plan of simplification, but includes a pancreatic anastomosis. Because of the short loop between the common bile duct anastomosis and the gastric anastomosis, it seems to us that it fails adequately to insure against reflux from the stomach into the biliary tract.

Numerous other procedures have been published, but they seem not to be crucial in the development of the ideal operation. An excellent summary of them is given by Orr.[21]

The University of Minnesota operation: The operation which we have now gradually developed as standard at this clinic has resulted from our own ex-

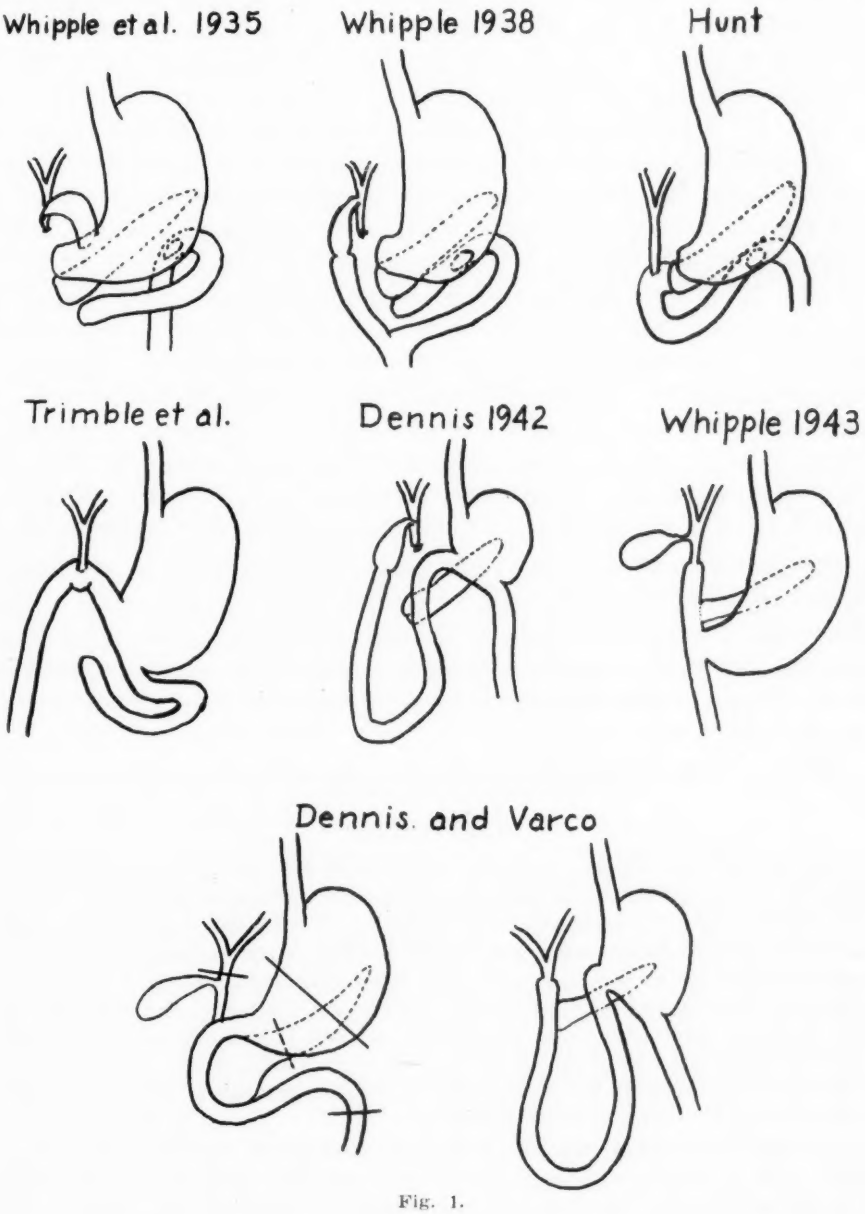

Fig. 1.

periences as much as from perusal of ideas expressed in the literature. A radical resection is performed, with removal of the distal third of the stomach, all the duodenum, the first 15 cm. of jejunum, about two-thirds of the common

bile duct, and the head, uncinate process, and neck of the pancreas in one block of tissue. The cut end of the remaining jejunum is temporarily closed and brought through the right side of the transverse mesocolon. The gall bladder is removed, and the cut end of either the common hepatic duct or the common bile duct is used for end-to-end anastomosis to the jejunum. In performing this anastomosis we employ fine silk as the suture material. As the jejunum passes the cut end of the pancreas, an anastomosis of the pancreatic duct to this viscus is made. At a point 40 cm. down the jejunum, a retrocolic Polya gastrojejunostomy is performed. Penrose drains are placed adjacent to the pancreatic and biliary anastomoses, and the abdomen is closed.

Anastomosis of the pancreas has been attempted by various maneuvers in the past. Coffey[18] attempted it by rather complicated plastic procedures on the bowel prior to implantation of the entire head, or tail, or the organ. He found the difficulty to be that tissue juices activate the proteolytic enzymes of the pancreatic juice, with resultant digestion of the vulnerable suture line. Poth[19] devised a silver button over which anastomosis could be made. Varco's method consisted in insertion of a catheter into the pancreatic duct, ligating it securely, and inserting it through a small stab wound into the intestine for 8 or 10 cm.[20] The anterior and posterior capsules of the pancreas are then sutured accurately to the serosa of the intestine about 1 cm. from the catheter entrance into the bowel. Such a scheme assures healing by delivering the proteolytic juice into the intestine at a distance from the healing suture line.

The Cancer Institute at the University of Minnesota has recently acquired a contact therapy machine by means of which areas not susceptible to surgical excision may be rapidly irradiated through the open wound. Five thousand roentgens (air) with a penetration of less than 1 cm. can be applied in 100 seconds. This has been employed in one case in this series and will probably be given further trial.

This final radical operation has been employed in six cases.

CASE REPORTS

CASE 1.—A. S., a 73-year-old woman, entered the Minneapolis General Hospital with a history of progressive painless jaundice and cardiac failure, which proved to be on an arteriosclerotic basis. Watson tests showed carcinomatous biliary obstruction. Following digitalization and cholecystostomy her condition very slowly improved on our usual preoperative regimen.[14] On Feb. 18, 1945, exploration was done. A well-localized lesion in the head of the pancreas was removed by the radical procedure described, but the gall bladder was left despite the presence of stones because it had been necessary repeatedly to await return of the pulse and blood pressure to normal levels, and gross transfusion had been feared because of the cardiac status. The postoperative course was surprisingly smooth, although she was slow to gain weight.

She returned to the Minneapolis General Hospital late in September with right upper quadrant pain in attacks. Passage of a gallstone into the common bile duct with impaction at the anastomosis was diagnosed and verified at operation, Oct. 10, 1945. The abdomen was free of evidence of tumor. The gall bladder was removed and the stone pushed into the jejunum. The postoperative course was marred by some purulent drainage around a wick left in the operative site, but the incision healed nicely, and the patient remains well, afebrile, and free of jaundice.

CASE 2.—J. M., a 74-year-old man, came to the University of Minnesota Hospitals on April 3, 1945, with jaundice of six months' duration, associated at the onset with pain. He had had three previous operations on the biliary tract, the last in 1940. Watson tests four months earlier had indicated hepatitis, but on this admission extrahepatic obstruction was indicated. Exploration on April 17, 1945, revealed a cancer of the common bile duct involving the duodenum. Radical resection was done. The patient died suddenly, in forty-eight hours, of pulmonary embolism, proved at autopsy. (Note: This had been feared because of extreme preoperative lethargy. On another occasion the vena cava will be ligated.)

CASE 3.—J. S., a 66-year-old man, came to the University of Minnesota Hospitals Aug. 29, 1945, with a two-month history of painless jaundice. Studies indicated carcinomatous obstruction, and radical resection was done Sept. 13, 1945. The postoperative course was complicated by a biliary fistula which closed in a few days. He went home, feeling well, Oct. 6, 1945.

CASE 4.—M. J., a 66-year-old woman, came to the University of Minnesota Hospitals Oct. 10, 1945, with a four-month history of painless jaundice. Watson tests indicated a cancerous obstruction and at operation Oct. 19, 1945, a radical resection was done for carcinoma, apparently of the intramural common duct. Drainage was omitted. The postoperative course has been uneventful to date (three and one-half months).

CASE 5.—M. O., a 57-year-old woman, came to the University of Minnesota Hospitals Nov. 19, 1945, with a six-month history of three bouts of jaundice and right upper quadrant pain and complete remission of all symptoms and jaundice between these episodes. Liver function studies were within normal values; a cholecystogram indicated a nonfunctioning gall bladder. At the time of exploratory surgery on Jan. 24, 1946, a neoplastic process of the ampullary area was encountered, and a radical resection performed. Catheter drainage of the choledochojejunostomy anastomosis was carried out via the cystic duct. The postoperative course has been satisfactory to date (Feb. 1, 1946).

CASE 6.—H. A., a 74-year-old man, came to the University of Minnesota Hospitals on Dec. 2, 1945, with a five-week story of weight loss and increasing painless jaundice. The liver function tests were diagnostic of neoplastic biliary obstruction. On Dec. 14, 1945, a radical resection for carcinoma of the ampullary area and head of the pancreas was carried out. Catheter drainage of the choledochojejunostomy anastomosis via the cystic duct was employed. The postoperative course was uneventful.

The difficulties inherent in such radical procedures are many, but the ones which have bothered most are:

1. Exposure. We have come to use a long transverse incision plus a vertical upward extension from the center (Brunschwig incision). This is adequate and minimizes the need for retraction. All have healed primarily.

2. Establishment of operability. After exposure of the lesion, it is often impossible to determine whether it involves the wall of the portal vein or the superior mesenteric vein until the operator has been committed to resection by division of the pancreas or the stomach. Involvement of other vessels, as the hepatic artery or splenic vein, occurs only a little less frequently, but is less difficult to determine.

3. Dissection of the portal vein and superior mesenteric vein from the pancreas. These vessels are friable and are joined to the pancreas, which partially surrounds them, by numerous fine tributaries which bleed profusely if torn. Adoption of the coagulating current to control these vessels has facilitated this dissection enormously. Dissection is also rendered difficult by the frequency of neoplastic or inflammatory adhesion to the walls of these veins.

4. Vascular anomalies. These are apparently frequent. We have done one procedure in which the celiac axis was absent and the hepatic artery arose from the superior mesenteric artery and traversed the head of the pancreas; in another the portal vein crossed entirely in front of the neck of the pancreas.

Other phases of the operation are straightforward, but time consuming.

Carcinoma of the Ampulla of Vater.—In 1899 Halsted reported a case of successful excision of a carcinoma of the ampulla of Vater by a transduodenal approach, utilizing local excision of the lesion and reimplantation of the ducts into the resulting defect in the mucosa of the posterior duodenal wall.[21] To date, this procedure has not been superceded. The single difficulty lies in failure to remove a wide block of tissue surrounding the lesion. A further practical difficulty sometimes has arisen here, namely, that more than the mucosa of the posterior duodenal wall may have to be removed, leaving a defect which is difficult to close.

Palliative Procedures.—Our experience has confirmed the impression that life can be prolonged and made more comfortable in the patients with frankly inoperable lesions. Following consistent failure in our hands of the stoma to remain patent after anastomosis of the gall bladder to the stomach or duodenum, we have come to employ routinely an end-to-end cholecystojejunostomy, or an end-to-end choledochojejunostomy with a modified Roux Y-plasty of the intestine. None of these has closed or leaked, and there has been no case of cholangitis.

Several of these patients have already developed duodenal obstruction at the time of the palliative operation, and some of them have developed obstruction after successful cholecystenterostomy. We are therefore inclined to favor gastrojejunostomy in addition to the biliary anastomosis as a part of the palliative procedure.

Through the use of these combined procedures rather than the more commonly employed simpler procedures, we feel that longer and better palliation has been obtained, and the operative risk seems to be no higher than for exploration alone.

SUMMARY OF CASES

In the period from Jan. 1, 1937, to Feb. 1, 1946, we have been able to find forty-six patients with biliary tract obstruction due to cancer who have passed through the main operating room at the University of Minnesota Hospitals and the Minneapolis General Hospital. Several other patients who arrived in terminal condition, or were not subjected to surgery for other reasons, are not included. The mortality rate of exploration in the twenty-three lesions found to be nonresectable has been higher than one might have expected. One-third of the nine patients having exploration alone failed to survive surgery. Twenty-one per cent of the fourteen given some sort of palliative procedure also died.

Those patients subjected to local excision of carcinomas of the common bile ducts or ampulla of Vater constitute the most gratifying group. There were nine altogether, with only one surgical death, the patient dying of hepatorenal syndrome.

Among the fourteen patients subjected to radical pancreaticoduodenectomy there were four deaths. One man, who had had an extensive carcinoma of the common bile duct removed, died of pulmonary embolus two days later. He had been very lethargic for many days before surgery, and embolus had been feared. We feel now that the vena cava should have been ligated at the time of resection. In another patient the hepatic artery arose from the superior mesenteric artery and traversed the head of the pancreas. It was reanastomosed too slowly to permit survival. In still another, the superior mesenteric artery was adherent to the mass and was accidentally cut. In the fourth patient the portal vein was found to be heavily involved after we had been committed to resection. A segment was excised and the ends were resutured; the anastomosis remained patent, but the patient died of hepatorenal syndrome.

One of the gratifying aspects of the radical resection and the local excision of the common duct in which the Allen[22] procedure was used has been the complete absence of cholangitis. Data on operative mortality are presented in Table I.

The late survival data of those patients undergoing local excisions of lesions of the ampulla are gratifying, the average being twenty-two months, with four of the five patients still alive. The outlook in the common duct obstructions proved to be less satisfactory, the mean survival being eight months. In the radical resections for whatever cause, the operative mortality was high enough to affect the mean survival rate considerably; the figure was three and one-half months (five months if the figures are derived from survivors of surgery alone) (see Table II).

Late survival in the group explored only or given palliative procedures has been partially studied, our follow-up data being incomplete. As will be seen in Table III, the mean survival in the patients with simple exploration for which we have information was only one month. In those given some palliation, it was but little better, three months.

TABLE I. IMMEDIATE RESULTS OF SURGICAL PROCEDURES FOR NEOPLASTIC BILIARY OBSTRUCTION

PROCEDURES AND SITES OF LESIONS	NUMBER OF PATIENTS	SURGICAL DEATHS
Exploration only		
Pancreas	6	2[1]
Gall bladder and common duct	1	1
Uncertain origin	2	0
Palliative procedures	14	3
Local resections		
Common bile duct	4[2]	1[3]
Ampulla of Vater	5	0
Radical pancreaticoduodenectomy		
Common bile duct	3	1[4]
Ampulla of Vater	3	1[5]
Head of pancreas	8[6]	2[7]
Total	46	11

[1]One died on induction of anesthesia alone.
[2]One, J. R. Paine; one, O. H. Wangensteen.
[3]Patient died of hepatorenal syndrome.
[4]Pulmonary embolus two days postoperative.
[5]Superior mesenteric artery cut accidentally.
[6]One by J. R. Paine.
[7]One case of vascular anomaly; one case of heavy involvement of portal vein found only after commitment to excision; segment resected and anastomosis attempted; anastomosis functioned and remained patent (proved at post-mortem), but patient died of hepatorenal syndrome.

TABLE II. FOLLOW-UP DATA ON PATIENTS WITH NEOPLASTIC BILIARY OBSTRUCTION

TYPE OF PROCEDURE	NUMBER SURVIVING SURGERY	SURVIVAL AND STATUS
Local excisions		
Common duct	3	Living and well 4½ mo.
		Dead 1 yr.
		Dead 15 mo.
Ampulla	5	Living and well 36 mo.
		Living and well 27 mo.
		Living and well 9 mo.
		Living 23 mo.
		Dead 10 mo.
Radical excisions		
Common duct	1	Living and well 3½ mo.
Ampulla	3	Living and well 2 mo.
		Living and well 1 mo.
		Dead 8 mo.
Pancreas	6	Living and well 12 mo.
		Living 6 mo.
		Dead 6 mo.
		Dead 5 mo.
		Dead 3½ mo.
		Dead 3 mo.

TABLE III. FOLLOW-UP DATA ON PATIENTS WITH NEOPLASTIC BILIARY OBSTRUCTION; SURVIVAL TIMES

PROCEDURE	NUMBER OF PATIENTS	MAXIMUM SURVIVAL	MEAN SURVIVAL
Exploration only	4	3 mo.	1 mo.
Palliation	12	11 mo.	3 mo.
Resections (local)			
Ampulla	5[1]	36 mo.	22 mo.
Common duct	4[2]	15 mo.	8 mo.
Radical pancreaticoduodenectomies	14[3]	12 mo.[4]	3½ mo.

[1]Four living.
[2]One living and well.
[3]Five living.
[4]Living.
Note: Figures include patients who were surgical casualties.

CONCLUSIONS

1. Our experience with forty-six patients with neoplastic biliary obstruction has been presented. Fourteen of these had radical pancreaticoduodenectomy, and nine had local excisions of the ampulla or common bile duct.

2. A procedure has been presented which we have evolved for the radical resections. For several reasons we consider it superior to any heretofore reported. The most important is the simplicity of the plan. Also important is the complete elimination of cholangitis in this series.

3. Thirteen new radical pancreaticoduodenectomies are added to the 104 cases already in the literature, one of which also came from this group.

4. Simple exploration carried a 23 per cent mortality in the nonresectable lesions and the survivors of surgery in this group lasted on the average a little less than three months.

5. Radical pancreaticoduodenectomy carried a 29 per cent mortality, mostly due to now-avoidable factors. Of the ten survivors five died in an average

of a little over five months, and five are living and well at periods up to twelve months.

6. Local resections of lesions of the common duct or ampulla of Vater incurred a mortality rate of only 11 per cent. The ampullary local resections group has lost one patient out of five, and two of three patients with common duct resections to survive surgery are still living.

7. With the experience which has now been gained the mortality rate in surgery for tumors causing extrahepatic biliary obstruction may be expected to drop to less than 10 per cent.

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EXPERIENCES WITH THE PAUCHET TECHNIQUE OF COLOSTOMY CLOSURE

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THE past six years of warfare have established, as never before, the value of colostomy in the surgical treatment of gunshot wounds of the large bowel. Consequently, today, even more so than after World War I, the problem of colostomy closure has assumed importance out of keeping with its place in civilian surgery. For the past two years, colostomy closure has been the most frequently performed abdominal operation in general hospitals in this country. In the past year, on a single general surgical section of moderate size, there have been seventy such operations performed, a figure which represents only a small proportion of the total number of such procedures being carried out in general hospitals throughout the country at the present time.

In military life, the surgeon is rarely permitted the luxury of closing a colostomy which he has made himself. Most frequently he is committed to closing a colostomy, the structural details of which remain a well-guarded secret until revealed by operation or catastrophy. The elective colostomy of civilian surgery made under ideal conditions, and with a proper regard for surgical fundamentals, lends itself easily to the classical two-stage Paul-Mikulicz procedure of closure. The colostomy of military surgery made as an emergency measure under operating conditions far from ideal, and upon a shocked and mutilated patient, is frequently unorthodox or defective. In many instances such a defective colostomy can be properly evaluated prior to closure by careful and thorough examination, but in a surprisingly high proportion of patients even gross deformities or dangerous complications are revealed only at the time of the operative closure itself. Among the commonly encountered problems are the following: subcutaneous herniation of bowel; complete absence of spur; interposed foreign bowel or mesentery between the colostomy limbs; varying degrees of rotation of one limb of the colostomy around its fellow; secondary perforations or fistulas adjacent to the colostomy; and inflammatory or granulomatous masses involving the colostomy. Most of these complications prohibit, or make extremely hazardous, the employment of the Paul-Mikulicz technique of closure, with its preliminary spur crushing. In addition, in many cases, especially where the wound of entrance of a missile has been utilized to bring out the colostomy, musculofascial defects in the abdominal wall exist. The anatomic repair of these defects, which is essential if subsequent hernia is to be prevented, necessitates an intraperitoneal type of closure of the colostomy, which cannot be satisfactorily attained with the usual Paul-Mikulicz technique. These

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difficulties have been surmounted in various ways by various surgeons, the most common procedure being resection of the colostomy and end-to-end anastomosis, a procedure which we have ourselves employed on numerous occasions. However, in dealing with colostomies in the left colon and especially in the sigmoid colon by this method, a degree of functional obstruction at the site of the anastomosis frequently results, due either to postoperative edema or to the turning in of too much bowel wall in an overzealous attempt to construct a watertight, leakproof anastomosis (Fig. 1). This is especially true of the so-called "aseptic"

Fig. 1.—Barium study at four weeks after operation, revealing marked stenosis following resection of colostomy and end-to-end anastomosis, which has so far remained clinically silent.

anastomosis done over crushing clamps. During the first four or five postoperative days when the integrity of the suture line is menaced by distention within the bowel, this factor of temporary obstruction at the anastomosis becomes a very real hazard. It adds to the risk of leakage and failure of the closure and contributes significantly to the discomfort of both patient and surgeon, making necessary in a great many cases the withholding of food for sev-

eral days, suction decompression, frequent low enemas, and other nuisances. Again, several weeks later, barium studies reveal in a surprisingly great number of these patients a rather marked stenosis of the bowel at the point of anastomosis, which may or may not become of clinical significance later in the individual's

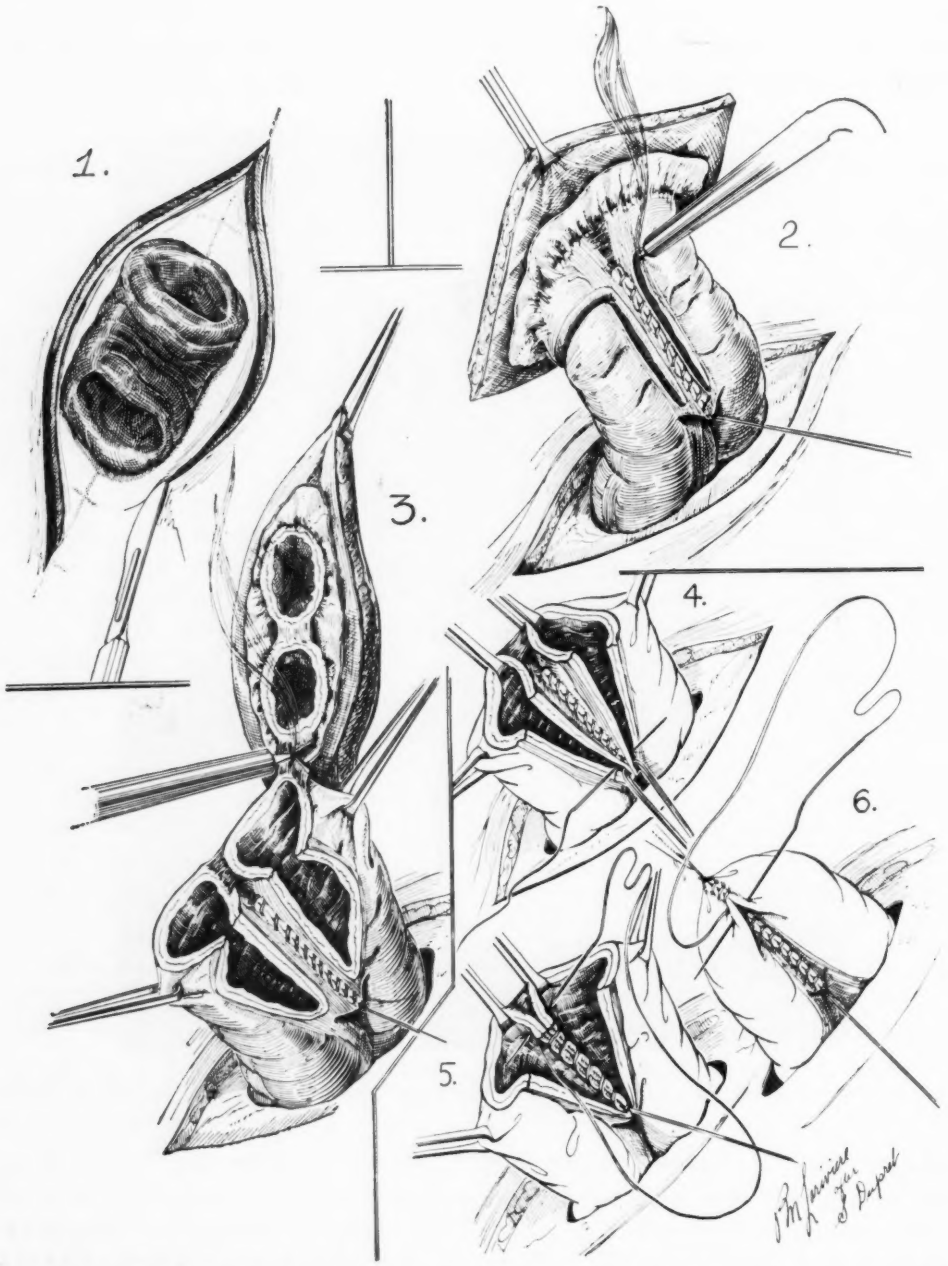


Fig. 2.—Pauchet technique of colostomy closure. The continuous suture shown in *5* is usually continued down the lateral aspect of the anastomosis as a continuous Connell stitch in our technique. Interrupted Halsted sutures of fine black silk are usually substituted for the continuous Lembert suture shown in *6*. Cautery is not used in our technique. (From Maingot, Abdominal Operations, Vol. II, New York, N. Y., D. Appleton-Century Company, p. 1334.)

life. We propose, therefore, to describe a method of colostomy closure which in our hands has satisfactorily surmounted these difficulties in twenty-two consecutive cases. The technique was first described by Victor Pauchet in 1934, and has thus far not found favor with American surgeons, either because of unfamiliarity or because of its apparent lack of simplicity.

TECHNIQUE

The operation embodies largely the principle of the Finney pyloroplasty, and consists briefly in encircling the colostomy stoma by an elliptical skin incision, leaving a cuff of skin about one-quarter inch around the mucosal edge. The incision is deepened in an anatomic manner by sharp dissection through all the layers of the abdominal wall down to the peritoneum, which is then deliberately opened along the medial aspect of the colostomy. The peritoneal incision is continued by sharp dissection so that it completely encircles and frees the afferent and efferent limbs of the colostomy. With gentle traction on the bowel, further mobilization is continued as far as is necessary to provide an adequate length of bowel for the anastomosis, and to permit, if necessary, resection of the colostomy or of segments of bowel deformed by secondary fistulas or stomata, extensive scarring or granulomatous masses. Proper mobilization permits complete delivery from the abdominal cavity of the afferent and efferent limbs of bowel to be used in the anastomosis. The wound edges and the peritoneal cavity are protected by two large saline packs tucked snugly down into the wound around the bowel. All subsequent surgical procedures are then carried on entirely outside the abdominal cavity and the operative wound. After such complications as bowel rotation and interposition of small bowel or omentum, etc., are corrected, and after resection of undesirable segments of bowel has been completed, the anastomosis is performed as shown in the illustrations (Fig. 2). Upon completion of the anastomosis the bowel is carefully replaced within the peritoneal cavity so as to avoid twisting or kinking, and the wound is then closed in layers without drainage. Depending on the individual desires of the surgeon, sulfonamide crystals may or may not be dusted into the wound, over the suture line in the bowel, and into the peritoneal cavity. It is our personal opinion that such solicitude is unnecessary. See Figs. 1 to 6.

RESULTS

The results following the employment of this procedure in twenty-two consecutive colostomy closures are presented in Table I.

COMMENT

In all of the patients in this series, thorough preparation of the bowel preoperatively with sulfasuxidine and a low residue diet was done. The effectiveness of sulfasuxidine preparation was not checked by stool cultures, but it was noted that for two or three days prior to operation the stools became soft, brownish yellow, and odorless, phenomena which have been described by many investigators. On the night before operation all patients received irrigations of 1,000 c.c. of tap water in the afferent and efferent loops of the colostomy, follow-

TABLE I. SIGNIFICANT FEATURES IN TWENTY-TWO CONSECUTIVE COLOSTOMY CLOSURES BY PAUCHET TECHNIQUE

PATIENT	LOCATION OF COLOSTOMY	TYPE OF COLOSTOMY	ASSOCIATED DEFECTS AND COMPLICATIONS	SUITABLE FOR MIKULICZ CLOSURE?	ADDITIONAL SURGICAL PROCEDURES NECESSARY AT CLOSURE	POSTOPERATIVE COMPLICATIONS
E. N.	Sigmoid	Double-barreled, no spur	Prolapsed distal loop	No	Reduction of prolapse	None
R. P.	Transverse colon	Exteriorization, no spur	None	No	None	None
E. B.	Transverse colon	Exteriorization, no spur	Large hernia at colostomy site	No	Extensive repair of abdominal wall	Postoperative incisional hemorrhage
G. F.	Transverse colon	Exteriorization, spur type	None	Yes	None	None
G. C.	Transverse colon	Exteriorization, spur type	None	Yes	None	None
O. E.	Sigmoid	Exteriorization, spur type	None	Yes	None	None
V. G.	Sigmoid	Exteriorization, spur type	Short spur, rotation of loops	No	Correction of rotation	None
H. H.	Sigmoid	Double-barreled, spur type	None	Yes	None	Rectal hemorrhage, third postoperative day due to deficiency controlled with vitamin K
L. G.	Sigmoid	Double-barreled, spur type	Subcutaneous herniation, both loops	No	Repair of musculofascial defect	None
L. M.	Transverse colon	Tangential, loop type	No spur, adherent loops small bowel	No	Separation of adherent small bowel	None
F. T.	Descending colon	Exteriorization type	Multiple stomata; bowel rotation; fecal fistula from afferent loop	No	Resection of colostomy and four inches of colon	None
J. F.	Transverse colon	Exteriorization with spur	Hepatocolic fistula	No	Closure of hepatocolic fistula; resection of colostomy	None

ing which they were given 8 c.c. of paregoric by mouth. This dose was repeated on the morning of operation. Invariably, at operation the bowel was found to be completely and shiningly clean, containing no fecal matter or residue of any kind. Primary wound closure without drainage was performed in all but one patient, in whom a small Penrose drain was left for thirty-six hours down to the site of closure of an associated hepatocolic fistula. All wounds healed kindly without induration or reaction in every case but one, which will be discussed later. There were no evidences of wound infection or drainage in any patient.

The patients were allowed to take a full liquid diet as soon as they returned from the operating room. All were ambulatory on the first postoperative day, and had normal bowel movements without cramping, enemas, or cartharsis on the second or third postoperative days. All patients were taking a regular house diet on the third postoperative day. In no case was postoperative suction decompression employed or thought necessary. Sulfasuxidine was continued for

TABLE I—CONT'D

PATIENT	LOCATION OF COLOSTOMY	TYPE OF COLOSTOMY	ASSOCIATED DEFECTS AND COMPLICATIONS	SUITABLE FOR MIKULICZ CLOSURE?	ADDITIONAL SURGICAL PROCEDURES NECESSARY AT CLOSURE	POSTOPERATIVE COMPLICATIONS
F. B.	Sigmoid	Double-barreled, spur type	Short spur	No	None	None
D. J.	Sigmoid	Exteriorization, no spur	Mucosal herniation, no spur, bowel rotation, accessory stoma in proximal loop, extensive scarring	No	Resection of colostomy and 6 inches of colon	None
E. R.	Sigmoid	Double-barreled, spur type	None	No	None	None
A. K.	Sigmoid	Double-barreled, spur type	None	Yes	None	None
B. B.	Sigmoid	Tangential loop type	No spur, stenosis and scarring	No	None	None
J. W.	Sigmoid	Double-barreled, spur type	None	Yes	None	None
B. D.	Sigmoid	Double-barreled, spur type	None	Yes	None	None
P. C.	Sigmoid	Tangential	No spur	No	None	None
C. E.	Sigmoid	Double-barreled, spur type	None	Yes	None	None
J. E.	Sigmoid	Double-barreled, spur type	None	Yes	None	None

five days postoperatively in two patients, in whom extensive bowel resection had been necessary. None of the remaining nineteen received sulfasuxidine postoperatively. There were no instances of failure or partial reopening of the closure. Barium studies done in each case from three to four weeks postoperatively revealed extremely adequate, and at times very large, bowel lumens at the site of anastomosis. (Figs. 3 and 4.)

DISCUSSION

The method of colostomy closure originally described by Pauchet was intended solely for reconstruction operations on the left colon, especially in the region of the sigmoid. Our experience has extended the application of the procedure to the transverse colon as far proximally as the hepatic flexure. We have not employed the method for reconstruction of the right colon since in this location resection and end-to-end anastomosis leaves nothing to be desired because of the anatomic characteristics of the bowel and the fluid nature of its contents. The advantages of the method as we see it, are as follows:

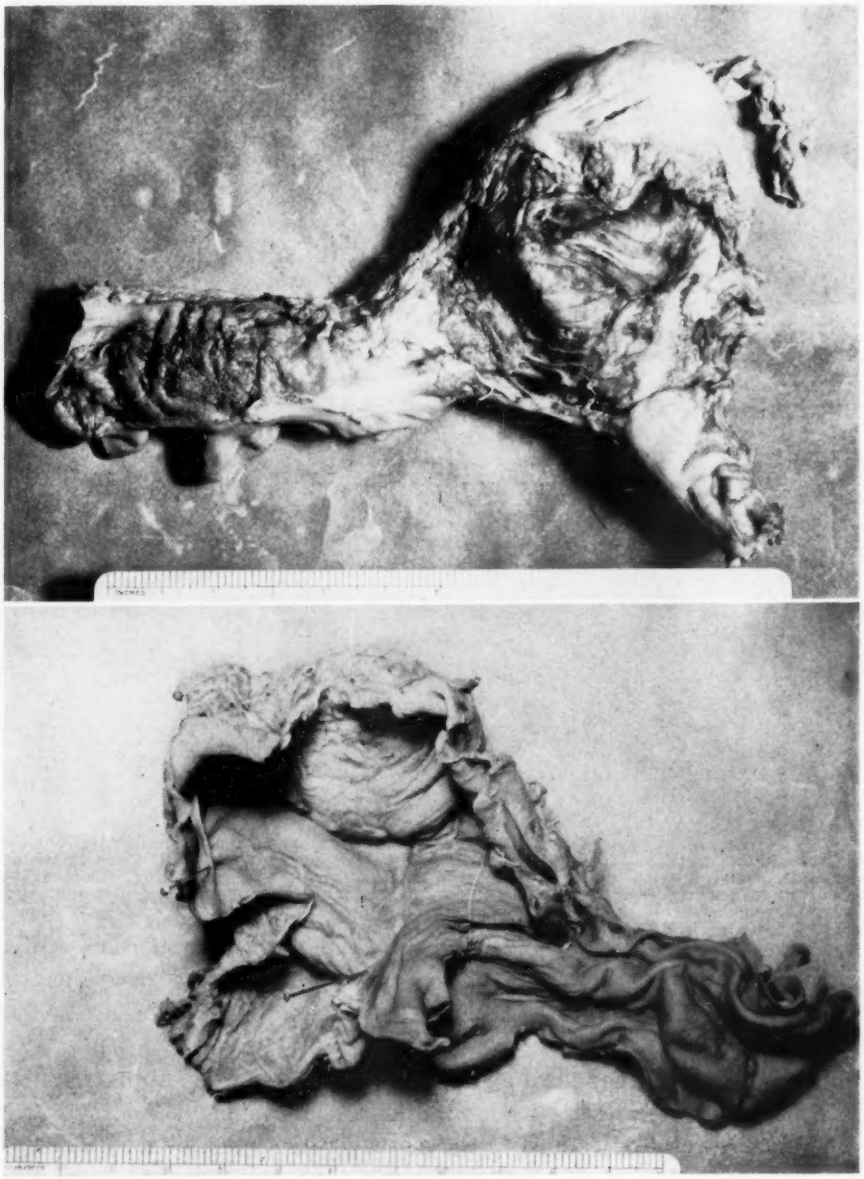
1. In common with resection and end-to-end anastomosis, the Pauchet technique of colostomy closure in one stage eliminates the waste of time and the

Fig. 3, *A* to *D*.—Barium studies of four typical cases, four weeks postoperatively, showing ample lumens obtained following colostomy closure by Pauchet technique.

dangers entailed in the crushing of a spur which may be badly formed, short, defective, or actually absent.

2. The actual surgical procedures upon the bowel itself, including resection of undesirable bowel, anastomosis, etc., are carried on outside of the abdominal cavity and in fact, for the most part, outside of the operative incision.

A.



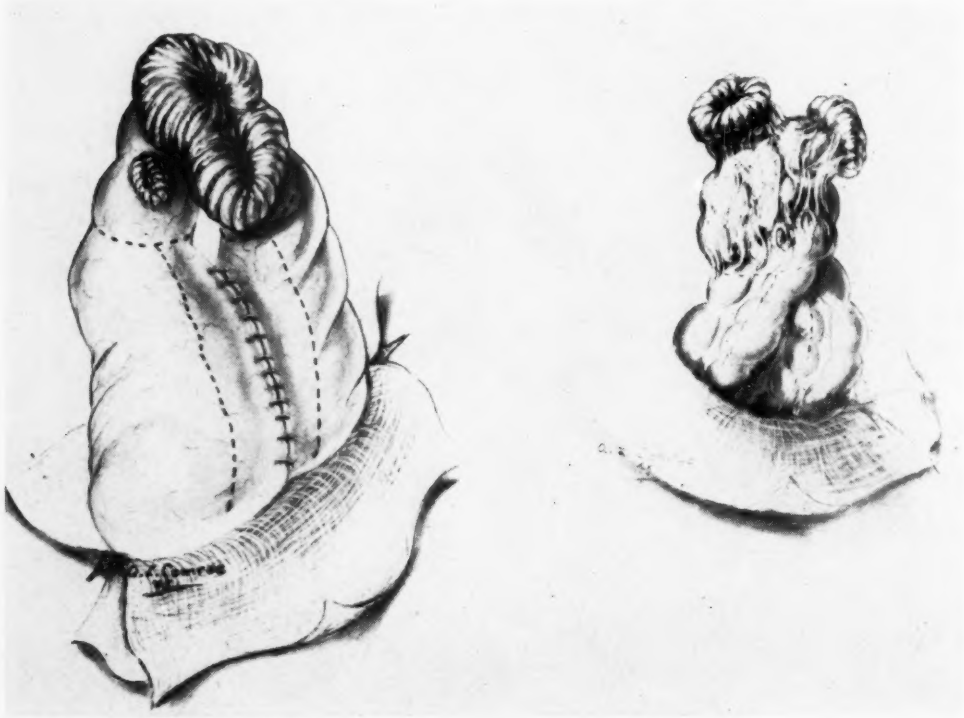
B.

Fig. 4, *A* and *B*.—Fixed autopsy specimen of colon in which a Pauchet colostomy closure had been done two months earlier, on a patient with severe bilateral renal lithiasis and infection, uremia and hemiplegia. Closure was done simply as a palliative procedure to make the patient's last few months of life more comfortable and to relieve family of nursing care associated with colostomy. Patient died of inanition following status epilepticus. *A*, serosal aspect; *B*, mucosal aspect.

3. A safe method of intraperitoneal closure is provided making possible a thorough anatomic repair of the operative incision, in layers, without drainage, resulting in a firm, well-healed abdominal wall, in which the development of hernia is extremely unlikely.

4. The method is extremely adaptable to the closure of defective, deformed, or otherwise complicated colostomies (Fig. 5).

5. An adequate, even generous, lumen is provided at the site of anastomosis (Fig. 3).



A. *B.*

Fig. 5.—Showing adaptability of Pauchet technique to closure of complicated colostomies. *A*, Accessory stoma and fecal fistula involving distal limb of colostomy. *B*, Case in which 180° rotation had occurred with extensive scarring and deformity of colostomy. Dotted lines in each case indicate levels of resection of colostomy and incisions for Pauchet anastomosis.

6. The postoperative morbidity is minimal, early ambulation and early feedings are permitted, and such postoperative nuisances as gas pains, partial obstruction, suction decompression, and the withholding of food are so far unknown.

7. It is suggested that the Pauchet procedure may well supplant the second stage of the obstructive resection for carcinoma of the sigmoid.

There are several objections to the method which must be mentioned. First of all, it is somewhat more time consuming than the standard Paul-Mikulicz procedure, although with experience the entire operation from beginning to end should consume no more than thirty minutes. When the procedure is complicated by the necessity for resection of a segment of bowel, more time is needed.

However, with fairly extensive resections of from six to eight inches of scarred, distorted, and adherent bowel, the total operating time has not exceeded ninety minutes, and is usually about sixty minutes.

Second, as compared to simpler methods of anastomosis or closure, such as end-to-end suture, or the Paul-Mikulicz procedure, it is apparent that an excessive amount of suturing must be done, and that a rather long suture line will result which theoretically enhances the possibility of leakage. This theoretic possibility has not become an actuality in our experience. These bad features are, we think, more than compensated for by the fact that, with the extremely generous lumens which are possible with this method, the surgeon can make a very firm, leakproof anastomosis, without fear of obstruction or stricture, by turning in a fairly large cuff of bowel wall all around, using two, or even three, layers of sutures.

Fig. 6.—Barium study done three weeks after operation, demonstrating a common error in Pauchet closure. Note large lumen, but also distal kinking due to rotation of gut caused by (a) using too much bowel in an effort to make unnecessarily large lumen; (b) making anastomosis medially rather than laterally as described.

In making anastomoses by this method certain precautions are necessary. The surgeon should beware of utilizing long segments of bowel in an effort to create an unnaturally and unnecessarily large lumen. If this is done, kinking or torsion may result just proximal and just distal to the anastomosis when the bowel is replaced within the peritoneal cavity. This occurred to a minor degree in one of our patients, but fortunately caused no apparent discomfort or complications (Fig. 6). It is usually preferable to follow the original technique of Pauchet and make the anastomosis laterally, reflecting the mesocolon medially toward the abdominal cavity. This prevents the development of tension when

the last or outer suture layers are being placed. If one encounters at operation a spur which was previously formed by rotating the anterior taeniae of the two limbs medially in the customary manner, this should be thoroughly disconnected. The bowel should then be rotated laterally and the anastomosis made laterally, as described. After the incisions in the bowel wall have been thoroughly developed and are ready for suture, the cut edges should be accurately aligned by means of Allis clamps. If this is not carefully done, serious distortion of the suture line may result.

Two interesting postoperative complications deserve to be mentioned. In one patient rather extensive rectal bleeding occurred on the second postoperative day. Prothrombin determinations revealed an extremely low level of circulating prothrombin (less than 10 per cent) which was quickly corrected by the intravenous administration of 2-methyl-1,4-naphthoquinone with prompt, complete, and permanent cessation of the bleeding within two hours. In the second case an extensive repair of a musculofascial defect in the abdominal wall was done. This patient developed a postoperative incisional hemorrhage on the second day. In this patient, also, an extremely low prothrombin level was discovered which, when corrected by intravenous administration of 2-methyl-1,4-naphthoquinone, resulted in prompt and permanent cessation of bleeding. In both of these cases, routine studies had shown normal prothrombin levels at the beginning of sulfasuxidine therapy seven days prior to operation. It is felt that the marked reduction of vitamin K-synthesizing colonic bacteria brought about by sulfasuxidine was partly responsible for these hemorrhagic phenomena. Since that time we have routinely administered synthetic vitamin K by mouth, both preoperatively and postoperatively, in all patients receiving sulfasuxidine therapy and have encountered no subsequent instances of hemorrhage.

SUMMARY

1. A method of colostomy closure in one stage is described which is extremely adaptable to the closure of many types of orthodox, unorthodox, and defective colostomies in the transverse, descending, and sigmoid colons.

2. A series of twenty-two consecutive colostomy closures by this method, with no failures, and with minimal morbidity and complications, is presented.

3. This procedure is suggested as a substitute for the second stage of an obstructive resection for carcinoma of the sigmoid by the Paul-Mikulicz technique.

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THE TREATMENT OF PATIENTS WITH ACHALASIA BY ESOPHAGOGASTROSTOMY

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DERANGEMENT of function of the lower esophagus with dilatation of the upper esophagus and delayed passage or retention of food is a disease that has been described in the literature under various titles. The terms commonly used are cardiospasm or achalasia. Descriptive titles such as ectasia, idiopathic or paralytic dilatation of the esophagus, and megaesophagus have also been employed to emphasize enlargement of the upper esophagus. The condition has usually been treated by diet, drugs, and intraesophageal dilatation. Progressive dysphagia and starvation have occasionally necessitated surgical intervention for relief of obstruction.

Different operations have been proposed for this disease. Those designed to enlarge the opening between the esophagus and stomach are of interest to this report. Two of these operations avoided opening into the lumen of the esophagus. The first was performed in 1900 by Mikulicz[1] and consisted of a transabdominal manual and instrumental dilation of the cardia and lower esophagus. The second was used in 1914 by Heller.[2] Two longitudinal incisions, one anterior and one posterior, were made along the lower esophagus and down to the stomach. The muscles were divided but the mucosa was left intact. The operative procedure is similar to that used for congenital pyloric stenosis.

The first operation for achalasia that opened into the esophagus was evidently performed by Wendel.[3] In 1910 he made a single longitudinal incision into the lumen of the lower esophagus and continued it through the anterior wall of the cardia of the stomach. This longitudinal incision was then retracted laterally and sutured transversely to perform a cardioplasty. Heyrovsky[4] later reported an open operation also first performed in 1910 that brought the dilated portion of the esophagus down through the diaphragm. A side-to-side anastomosis was then made between the esophagus and the cardia of the stomach. The terminal portion of the esophagus, which was not enlarged, was not disturbed. In 1913 Lambert[5] enlarged the opening between the dilated esophagus and the stomach by inserting one blade of a long spur-crushing clamp into the lumen of either organs and crushing the adjacent walls. The clamp was brought out through a temporary gastrostomy and later removed. Gröndahl[6] in 1916 was evidently the first to modify the Heyrovsky esophagogastrostomy by using a technique similar to that employed earlier by Finney[7] for gastroduodenostomy. Bull,[8] Womack,[9] Ochsner and DeBakey,[10, 11] Gray and Skinner,[12] Scott,[13] Clagett, Moersch, and Fischer,[14] and others have discussed the use of this operation for achalasia. Favorable results have been reported.

This presentation deals with the use of esophagogastrostomy in patients with achalasia. For convenience the operation will be referred to as cardio-

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plasty. It was performed through an upper abdominal midline incision. After dividing the left triangular ligament and retracting the left lobe of the liver, the lower portion of the esophagus was mobilized and delivered into the abdomen. Care was taken to bring down the dilated segment. In Fig. 1 is illustrated the importance of extending the incision in the esophagus well up into the area of enlargement. A normal-sized segment of the lower esophagus as long as that illustrated is frequently observed between the stomach and the enlarged and thickened upper esophagus. An incision well into the enlarged area is necessary to insure adequate drainage. Fine interrupted catgut sutures were used for the anastomosis. There has been no operative mortality.

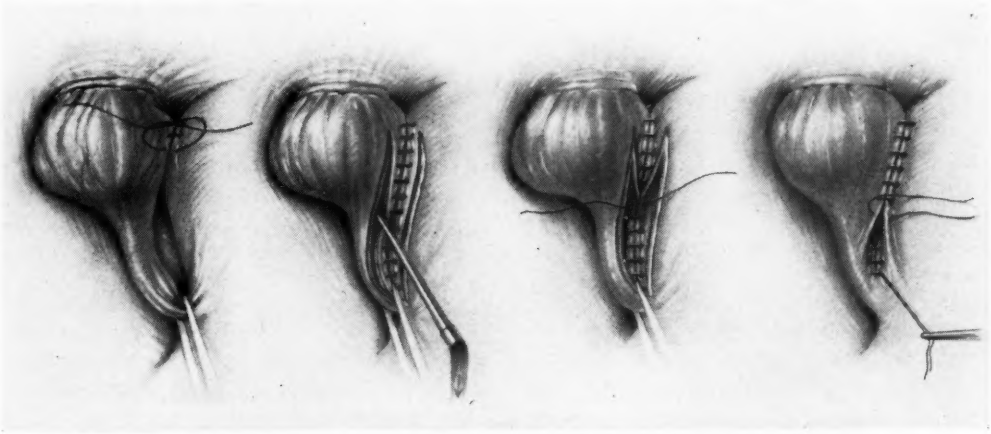

Fig. 1.—The drawings illustrate the importance of extending the incision for esophagogastrostomy or cardioplasty through the stomach and small lower esophagus into the enlarged portion of the esophagus to insure adequate drainage. Suction, rather than the use of temporary clamps or ties about the esophagus, facilitates upward extension of the incision.

Brief case histories of nine patients treated by this operation will be presented and changes in the size of the esophagus will be described. Also the effect of sympathectomy performed for hypertension, and the effect of vagotomy performed for peptic ulcer upon the function of the esophagus will be discussed.

CASE REPORTS

CASE 1.—E. R., a white man, was 47 years of age at the time of operation and had had dysphagia for nine months. He had lost forty of his usual 160 pounds of body weight. Six months before operation he was hospitalized for five weeks and treated by belladonna, diet, and repeated dilatations of the contracted lower esophagus. There was temporary relief of dysphagia with a gain of ten pounds in weight. Four months before operation swallowing became more difficult and episodes of regurgitation occurred. During the last ten days liquids passed into the stomach with difficulty. X-ray revealed an enlarged upper esophagus and a smooth narrow lumen near the cardia.

Transabdominal cardioplasty was performed July 29, 1941. Convalescence was uneventful. The patient ate a full house diet after eight days. Two weeks later a large piece of beefsteak completely obstructed the esophagus. Esophagoscopy was performed and the meat was removed. The patient then ate regularly and maintained a weight of around 170 pounds until June, 1945. At this time moderate dysphagia again developed. Fluoroscopic examination revealed rapid emptying of an esophagus of normal size. Esophagoscopic examination revealed some narrowing at the site of the anastomosis. Dilatation of this region was performed four times. Symptoms were relieved and the patient has continued to eat normally.

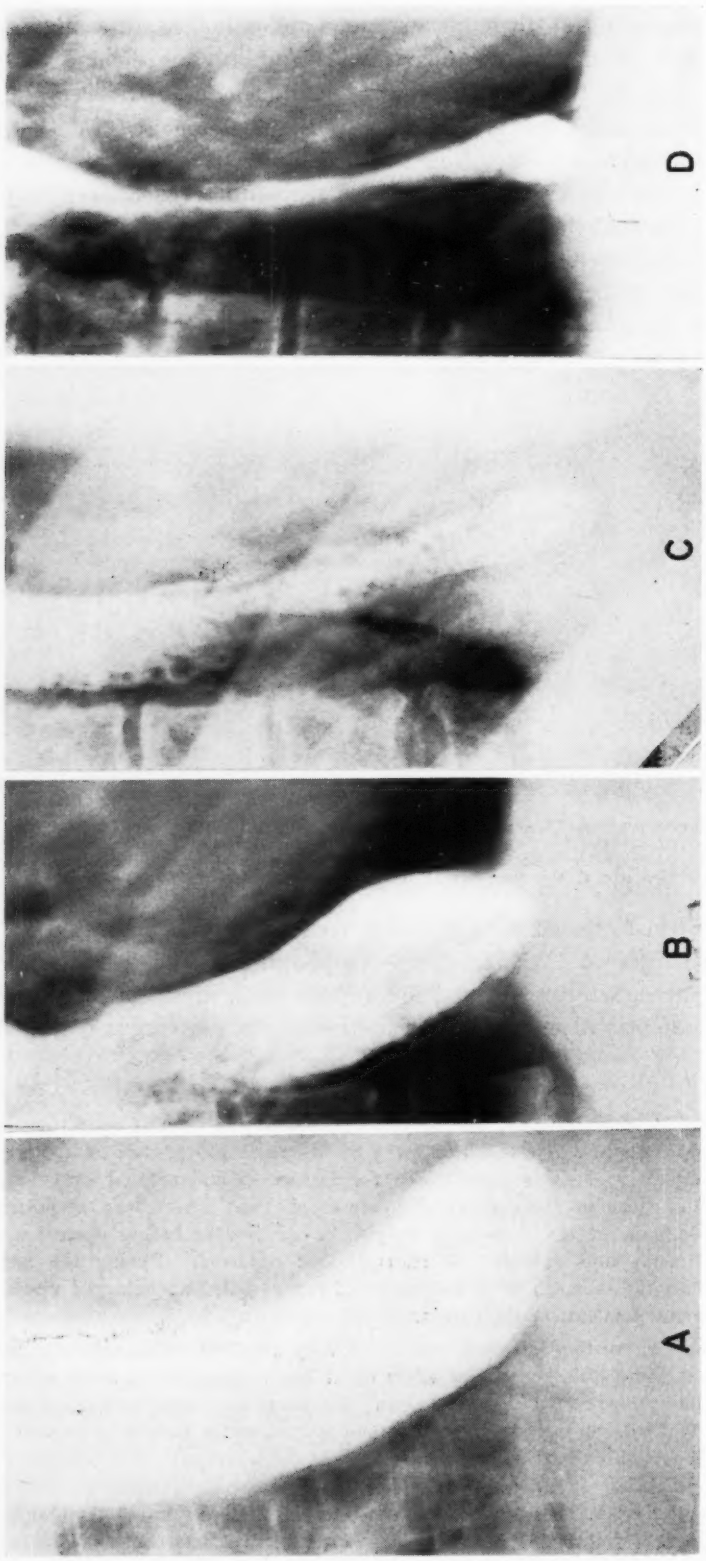

Fig. 2 (Case 2).—Roentgenograms reveal the appearance of the esophagus before cardioplasty (*A*). Progressive reduction of size is evident after thirteen days (*B*), nineteen months (*C*), and thirty-four months (*D*).

CASE 2.—H. W., a white man, was 21 years of age at the time of operation. He had had dysphagia for three years. Dilatations of the lower esophagus were begun when symptoms developed, and continued two or three times a month for one and one-half years. Relief of symptoms after each dilatation lasted one or two days. Dilatations were then performed at less frequent intervals up to the time of operation. During the last year drugs and psychotherapy were also employed. Regurgitation occurred several times a day. The weight of the patient decreased from around 132 to 127 pounds. Examination of the esophagus by x-ray revealed marked dilatation of the upper portion and smooth narrowing of the cardia.

Cardioplasty was performed March 5, 1943. Convalescence was uneventful. Within ten days the patient tolerated a regular diet. He did not have dysphagia for twenty-five months. Difficulty then occurred on several occasions after eating tough steak. Although fluoroscopy at this time revealed that barium passed readily, esophagoscopy revealed granulation tissue at the site of the anastomosis. This was cauterized. Three dilatations at intervals of one month again effected relief of dysphagia. Thirty-three months after operation an anemia was noted and three blood transfusions were given by a local physician. There was no history of melena or hematemesis. The patient's weight increased to 146 pounds. X-ray examinations (Fig. 2) revealed decrease in the size of the esophagus until at thirty-four months the diameter was normal.

CASE 3.—E. H., a white girl, was 17 years of age and weighed 105 pounds at the time of operation. Difficulty in swallowing had been present since birth. The first symptom was a choking sensation, that was occasionally associated with dyspnea, after eating. During childhood the patient would drink water, press on the lower neck, and occasionally vomit to relieve this choking sensation. During the last five years symptoms progressively became more severe. Regurgitation of some food occurred after each meal. Belladonna and other antispasmodic drugs, and on three occasions dilatation of the lower esophagus, failed to relieve symptoms appreciably. X-ray revealed marked dilatation of the esophagus and obstruction to the passage of barium.

Cardioplasty was performed, June 8, 1943. At operation a band of fibrous tissue was discovered across the esophagus near the stomach. This did not seem to cause obstruction. It was divided and the anastomosis was completed. Convalescence was uneventful. Symptoms of dysphagia were relieved. Four months after operation an epigastric burning sensation was noticed after meals. This was relieved by taking soda. During the next two months fatigue developed and the patient was found to have a hemoglobin of 39 per cent. Esophagoscopy revealed that the anastomosis was adequately open but that there was friable granulation tissue at its upper end. There was no history of melena or hematemesis. A benzidine test revealed blood in the first stools. The anemia responded to treatment by feosol and vitamins. Later, during the time of the patient's marriage, occasional mild dysphagia was again noted. Dilatation was performed without relief. The dysphagia cleared up spontaneously shortly after the wedding ceremony. The patient's weight increased to 115 pounds. There was a change in size of the esophagus evident during x-ray examinations. Seven months after operation the caliber was normal and there was no delay in the passage of barium into the stomach. The findings thirty-one months after operation were the same.

CASE 4.—T. O., a 50-year-old white man, had had dysphagia and a choking sensation for three years. Regurgitation occurred frequently. During the last year there was a decrease in weight from 125 to 105 pounds. Dysphagia was more severe during this year and regurgitation occurred after most meals. Treatment by antispasmodic drugs and sedatives was ineffectual. Esophagoscopy and x-ray examination revealed dilatation and delay of emptying of the esophagus.

Cardioplasty was performed Nov. 6, 1943. A diseased gall bladder was also removed. The only difficulty in swallowing since operation has been an occasional delay of passage of lean meat. Regurgitation has occurred on two occasions. The patient eats heartily and has gained 27 pounds. X-ray examinations reveal the change in size of the esophagus. Thirty-seven months after operation the diameter was normal and barium passed freely. A dilatation was nevertheless performed to aid the swallowing of lean meat.

CASE 5.—O. J., a colored girl, was 16 years of age at the time of operation and had had difficulty in swallowing food and frequent regurgitation for four and one-half years. During the last year before operation her weight decreased from 113 to 93 pounds. Treatment before operation consisted of psychotherapy, sedatives, belladonna, and, on five occasions, dilatation of the lower esopahgus. X-ray revealed massive enlargement of the upper esophagus with a smooth contraction of the lower end that delayed emptying.

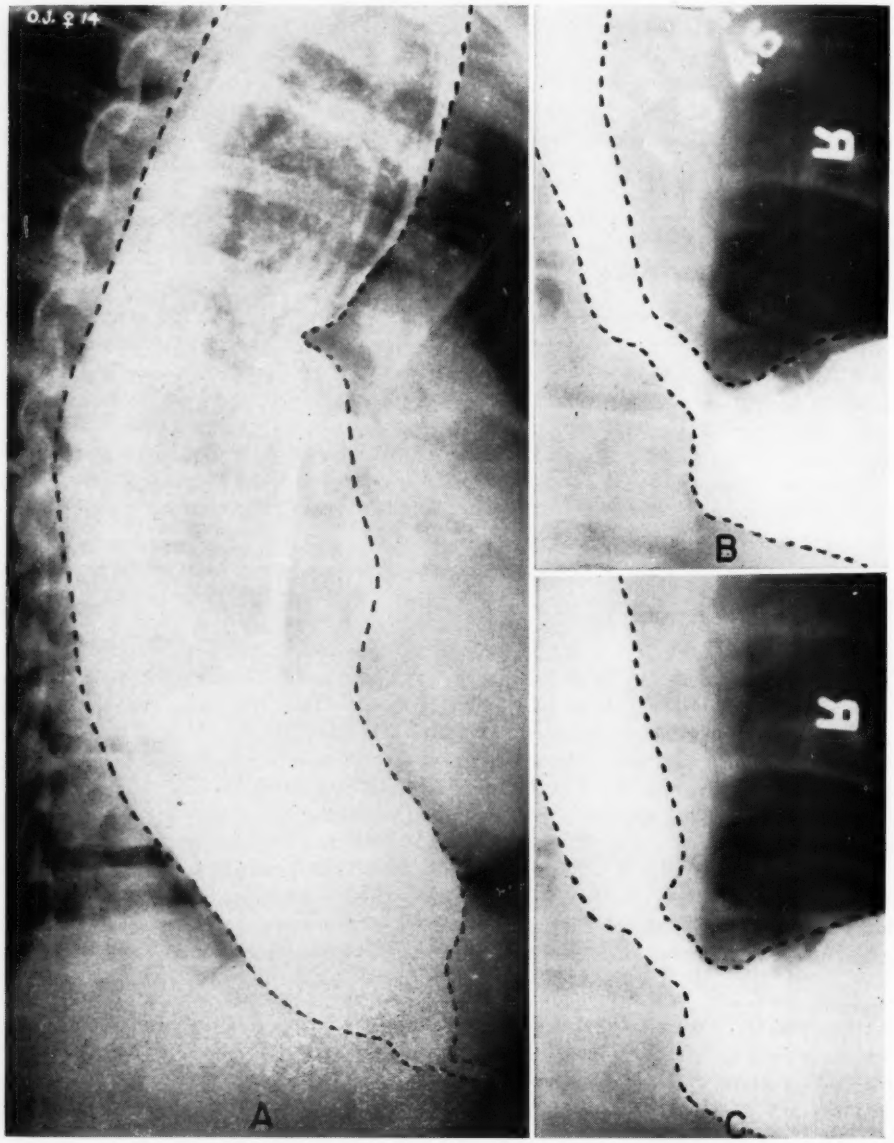

Fig. 3 (Case 5).—The dilatation of the esophagus present before operation (*A*) has reduced almost to normal eleven months after cardioplasty (*B*). Forced swallowing (*C*) reveals the site of the anastomosis at this time.

Cardioplasty was performed Feb. 8, 1944. The postoperative convalescence was uneventful. Dysphagia was relieved and within five months the weight was 136 pounds. Fig. 3 reveals the appearance of the esophagus by x-ray before operation and two views of the appearance of the lower esophagus and the anastomosis eleven months afterward. Fluoroscopy

at this later date revealed rapid emptying and little dilatation. The local physician reported that, twenty-three months after operation, the patient was eating regularly without difficulty.

CASE 6.—M. B., a colored woman, was 66 years of age at the time of operation. She complained that she had not been able to keep food down for thirteen years. Prior to this period her weight ranged around 270 pounds. During the thirteen years there was a weight loss of about ten pounds a year. During the month before operation the patient remained entirely in bed to conserve her strength. The weight on admission was 90 pounds. An esophagoscopy was attempted but discontinued because of massive regurgitation. X-ray revealed enlargement of the esophagus to an approximate diameter of three and one-half inches and marked delay of passage of barium.

Cardioplasty was performed Dec. 26, 1944. The postoperative course was uneventful. Fourteen days after operation a full house diet was well tolerated. The patient gained weight rapidly and ate without difficulty. Seven months after operation she returned because of pain in the left shoulder. Examination revealed an osteolytic lesion in the sixth cervical vertebra. Fluoroscopy revealed some dilatation of the esophagus. There were no pulmonary metastases. The patient did not return for further examination or treatment. The local physician reported that she died at home five months later with a large tumor mass in the left neck. Emaciation developed during the last two months and difficulty in swallowing developed during the last ten days.

CASE 7.—C. F., a colored woman, was 49 years of age at the time of operation. Dysphagia had been troublesome for six years. Two years before operation substernal discomfort developed with each meal. It was relieved by taking soda or drinking several glasses of water. Beginning one year before operation, swallowing produced a choking sensation and regurgitation occurred frequently. Esophagoscopy and x-ray revealed enlargement of the esophagus with angulation to the right and obstruction to the passage of barium. The patient had lost weight and at the time of operation weighed 116 pounds.

Cardioplasty was performed, May 12, 1945. There was an uneventful convalescence. During the eight months that have elapsed since operation, the patient has eaten with little difficulty. There has been no regurgitation, although at times the patient describes a rancid taste in the mouth. She complains only that strong coffee goes down slowly. There has been a gain of twelve pounds in weight. Examinations of the esophagus by x-ray reveal that there has been no appreciable decrease in the degree of dilatation or improvement in the rate of passage of barium after the operation. The narrowing of the esophagus, which was below the level of the diaphragm before operation, is now definitely above the diaphragm and above the level of the anastomosis. Dilatation of this area has been recommended.

CASE 8.—T. R., a colored man, was 29 years of age at the time of operation. Dysphagia began at the age of 14. X-ray examination seven months after the development of the illness revealed moderate dilatation of the esophagus and marked delay in the passage of barium. Esophagoscopy then confirmed a diagnosis of achalasia. Three dilatations effected some relief of symptoms. The relief lasted for three months. The patient was next examined at the age of 29. During the fifteen-year interval there had been continuous difficulty in swallowing. The patient forced all of his food down by drinking water. He frequently regurgitated and had to eat again. On two occasions emesis contained blood. Twice during the three months before operation the esophagus blocked completely for several days. X-ray revealed a dilated esophagus. At the time of operation the weight was 134 pounds.

Cardioplasty was performed, Aug. 4, 1945. The postoperative course was uneventful. During the six months that have elapsed since operation, the patient has gained nine pounds. He states that he can eat anything and that he experiences no difficulty. X-ray examination shows that the esophagus three months and six months after operation is only slightly enlarged.

CASE 9.—M. D., a colored woman, was 22 years of age at the time of operation. She described the first symptom as a sensation of fullness in the throat. This was noticed one year before operation. The tonsils and adenoids were removed by a local physician without relief. During the year she was able to eat solid foods by forcing them down with water. Dysphagia became more severe and regurgitation occurred frequently. When referred to

the hospital she could swallow only liquids. Esophagoscopy and x-ray revealed great enlargement of the upper esophagus and delay of passage of barium. The patient had lost weight from 124 to 105 pounds.

Cardioplasty was performed, Oct. 17, 1945. The postoperative course was uneventful. During the four months that have elapsed since operation the patient has eaten regular foods without difficulty and regained her usual weight. X-ray examination at this time reveals that the esophagus is reduced in size, although not yet normal.

SYMPATHECTOMY OF THE ENTIRE ESOPHAGUS

Subtotal to total paravertebral sympathectomy, splanchnicectomy, and celiac ganglionectomy[15] has now been carried out through a transthoracic approach in forty-nine patients as a treatment for hypertension. This procedure also removes the sympathetic nerve supply to the entire esophagus. The forty-nine patients have been followed several months to five and one-half years. The operation has not produced dysphagia or other symptoms of abnormal function of the esophagus. Templeton[16] studied the esophagi of eight of these patients by barium and fluoroscopy. Since then ten additional patients have also been studied by fluoroscopy and there has been no evidence of abnormal function.

VAGOTOMY OF THE LOWER ESOPHAGUS

Dragstedt and Schafer[17] have described a technique for removing the vagus nerves and branches about the lower esophagus that they have used as a treatment for peptic ulcer. This approach has been used for peptic ulcer in this hospital in twenty-seven patients now observed two to nineteen months. Examination of the esophagus and stomach by barium, x-ray, and fluoroscopy before and at intervals after operation has revealed no change in function. Patients have not developed dysphagia or other difficulty in swallowing. The motility of the stomach itself is decreased after vagotomy.

DISCUSSION

Various theories have been advanced to explain derangement of function of the esophagus and dilatation of the type described in the cases reported. These theories have been adequately reviewed by Bull,[8] Sturtevant,[18] Walton,[19] Womack,[9] Ochsner and DeBakey,[10] Gray and Skinner,[12] Scott,[13] Clagett, Moersch, and Fischer,[14] and others and will not be discussed in detail. The relationship between the observations in the patients described and the theories of causation of the disorder are of interest.

Dilatation of the esophagus, megaesophagus, and elongation and kinking of the esophagus, dolichoesophagus, have been considered primary factors in the disease. The possibility that the dilatation is acquired and results from atony or paralysis of the esophagus, esophagitis, or degenerative changes in the vagus nerves has received little support. Bull[8] credited von Hacher and Bard with the suggestion that dilatation of the esophagus might be a congenital malformation similar to megacolon or Hirschsprung's disease. Lendrum,[20] however, studied autopsy material and stated that kinking of the esophagus of the type now called dolichoesophagus was absent in all instances of early moderate dilatation and "can evidently occur only in cases of very old cardiospasm in which there has been lengthening as well as dilatation." Most of the reports published on the results of medical or surgical treatment have described only

moderate decrease in the degree of enlargement. Plummer[21] reported ninety-one patients treated by his hydrostatic dilator and stated that in three the esophagus returned to normal size.

A definite change in size of the esophagus after cardioplasty has occurred in eight of our nine cases. Four gradually decreased to a normal size, seven, thirty-four, thirty-seven, and fifty-three months, respectively, after operation. Two at three and eleven months were almost normal and two at ten days and three months had a significant reduction in size. One patient had no relief of obstruction and no decrease in size of the esophagus. These observations indicate to us that the dilatation in these cases was largely a result of chronic obstruction and therefore reducible by relief of obstruction. They do not indicate that in these cases the dilatation was of an idiopathic or congenital irreversible nature.

Cardiospasm has long been a popular term used to describe derangement of function of the esophagus being discussed. von Mikulicz[1] and Meltzer[22] probably originated the concept that a spasm at the lower end of the esophagus caused the disorder. Sturtevant[18] reviewed this literature and credited Lockwood with the suggestion that reflex irritation of the vagus nerves may be responsible. Lendrum[20] reviewed the literature indicating that cardiospasm might be associated with diverticulum of the esophagus, asthma, and more commonly with peptic ulcer. There were two healed duodenal ulcers in his thirteen autopsies. It is evident that emotional tension has at times temporarily aggravated symptoms in our nine patients. The disease of the gall bladder present in one of the patients described (Case 4) may also have reflexly influenced the degree of obstruction. There is, however, no evidence that emotional tension or reflex stimulation from abdominal disease caused the abnormality of function of the esophagus. Ochsner and DeBakey[10] found in the literature descriptions of eleven patients treated by vagotomy. The results were death in three, recurrence in seven, and improvement in one.

Rieder,[23] Knight,[24] Knight and Adamson,[25] and Ferguson[26] found that vagotomy in experimental animals produced a condition like that of "cardiospasm" or "achalasia." Our observations in twenty-seven patients before and after vagotomy for peptic ulcer revealed no significant disturbance of the function of the esophagus during the swallowing of food or barium.

Knight[27] also observed that sympathectomy in animals prevented the obstruction at the cardia that they believed was produced by vagotomy and advocated sympathectomy for "achalasia." Ochsner and DeBakey[10] reviewed reports of sympathectomy for "achalasia" including their own cases and stated that the results were not impressive. Our observations on the function of the normal esophagus after complete sympathetic denervation for hypertension have not demonstrated any significant change of function.

Scott and Morton[28] proposed spinal anesthesia as a test for overactivity of the sympathetic nerve supply to the colon. Telford and Simmons[29] and Scott[13] have reported improvement in "achalasia" or "cardiospasm" during and after spinal anesthesia. Interpretation of their results is difficult because of the multiplicity of the immediate changes effected by spinal anesthesia and the established difference between an acute and a chronic denervation of many body

structures. The observation, that chronic denervation of the esophagus of patients by sympathectomy or vagotomy does not appreciably alter peristalsis, supports the view that the myenteric plexus easily accomplishes motility by itself and may be only partially regulated by sympathetic and parasympathetic nerve impulses.

There are two major objections to the theory that there was a spasm of the lower esophagus in our nine cases. One is that of the nine patients none described pain referred from the lower esophagus, such as would be expected in spasm. The other objection is that examination during operation in all patients and biopsy in four revealed hypertrophy and thickening of the wall of the enlarged portion of the esophagus but not of the narrower portion. The narrower portion was elastic and grossly did not appear spastic.

Observations at the time of operation revealed that the esophageal hiatus of the diaphragm was adequately open. Since the junction of the small and the enlarged portion of the esophagus occurred at various levels and not always at the level of the hiatus it seems unlikely that a "diaphragmatic pinchcock" as described by Jackson[30] could have caused the disorder.

The term achalasia evidently originated in Guy's Hospital in London around 1913 when Hurst[31] investigated a patient and found that a rubber tube filled with mercury could be dropped through the esophagus into the stomach and withdrawn without meeting spasm or other appreciable resistance. He concluded from this and other studies that obstruction to the passage of food was not caused by cardiospasm but rather by "absence of relaxation of the sphincter." This sphincter he described as being normally about one inch in length. He stated that this sphincter is generally located at the level of the hiatus although it is occasionally lower and is rarely entirely thoracic. Rake[32] examined autopsy specimens from three patients with achalasia and found destruction of the ganglia and connecting nerves of Auerbach's plexus in the region of the sphincter and to a lesser degree in the dilated portion of the esophagus. This he believed was caused by inflammation and might be the primary lesion in achalasia. Lendrum[20] examined the myenteric plexus of the cardia of the esophagi in autopsy material from fifty-eight adults with grossly normal esophagi and stomachs and compared the findings with similar material from thirteen patients with achalasia. He observed that in each of the thirteen there was a striking loss or complete absence of ganglion cells from the myenteric plexus. The loss was as great in the undilated neck at the cardia as it was in the dilated portions. Lendrum also observed that there is a compensatory dilatation of the upper esophagus, and that as it becomes prodigiously dilated it is also stretched lengthwise so that bends and kinks may occur.

Unfortunately studies of the myenteric plexus were not performed during our study of nine patients treated by cardioplasty. It is, therefore, not possible to comment on these important histologic studies.

CONCLUSION

The evidence presented has led to agreement with many other authors that the term achalasia is proper for many patients with derangement of function of the lower esophagus. It seems to apply, although largely from negative evidence,

to the nine patients described. It also seems probable that the enlargement of the upper portions of the esophagus is produced by obstruction and retention and may be obviated by adequate relief of obstruction.

Acknowledgment is expressed to the Department of Surgery of the University of Chicago for the use of the record of Case 1.

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THE TREATMENT OF CARDIOSPASM BY ESOPHAGOGASTROSTOMY

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CARDIOSPASM is the term most frequently used to describe the syndrome in those patients who have more or less characteristic symptoms of dysphagia, regurgitation, and epigastric pain of long duration. The entity is not new, such cases having been reported as early as 1674, and the number recorded now exceeds 1,200. These cases are reported under many different designations, such as achalasia of the cardia, simple ectasia of the esophagus, paralytic dilatation of the esophagus, mega-esophagus, idiopathic dilatation of the esophagus, etc.

The etiology of cardiospasm is still in dispute. Some of the conditions to which it is attributed are primary apnea of the musculature of the esophagus, spasm of the cardia, failure of proper relaxation of the cardiac sphincter, spasm of the diaphragm, kinking of the esophagus, fibrosis of the periesophageal connective tissue, and autonomic imbalance.

Comparatively few cases have been reported in which operation has been performed in the attempt to relieve the condition. In 1930, Häggström[1] reported twenty-nine cases from the literature and added two of his own, making a total of thirty-one cases in which esophagogastrostomy was done by the transabdominal approach. No deaths occurred. At the same time he reported five cases in which operation was done by Sauerbruch by the transpleural route, with two deaths. Ochsner and DeBakey,[2] in 1940, reviewed the literature, collecting eighty-eight cases, and reported two of their own, in which esophagogastrostomy was done, bringing the total to ninety. In this group there were five deaths, or 6.6 per cent, and only one case in which the results were poor. These authors divided the operative procedures into four large groups depending upon whether they were directed at (1) the dilated esophagus, (2) the cardia, (3) the diaphragm, or (4) the nerve supply. Since their report there have been several other case reports in series of one to four. Clagett and associates[3] in 1945 reported four cases with good results.

Dilatation is the simplest procedure and should always be given a trial. Of all the different operative procedures which have been resorted to, esophagogastrostomy, first performed by Heyrovsky[4] in 1912, seems to us the most logical. The operation used by Heyrovsky was modified by Gröndahl[5] so that the technique is essentially the same as that used in Finney's gastroduodenostomy,[6] applied to esophagogastrostomy. We have operated on ten patients with cardiospasm by this technique (Figs. 1 to 5). In nine cases the transabdominal approach was used, while the transpleural route was utilized once (Table I).

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TABLE I. RECORD OF TEN PATIENTS TREATED BY ESOPHAGOGASTROSTOMY

CASE	AGE (YR.)	SEX	LENGTH OF HISTORY (YR.)	OPERATION	WEIGHT (LB.)	RESULT	FOLLOW-UP	
							YR.	WEIGHT (LB.)
1	21	F	10	Esophagogastrostomy	85	Excellent	2	128
2	36	F	10	Esophagogastrostomy	68	Excellent	2	118
3	54	F	12	Esophagogastrostomy	?	Excellent	1½	(Died of carcinoma of cervix)
4	35	M	4	Esophagogastrostomy	136	Excellent	2	150
5	74	F	2	Esophagogastrostomy	106	Excellent	1½	125
6*	53	M	4	Esophagogastrostomy	114	Fair	1½	124
7*	61	F	2	Esophagogastrostomy	116	Fair	1½	120
8†	37	F	2½	Esophagogastrostomy	130	Excellent	4½	190
9	56	M	14	Esophagogastrostomy	160	Excellent	1½	180
10	27	F	1	Esophagogastrostomy	104	Excellent	Operation Dec. 31, 1945; no follow-up	

*Reoperated upon (see Fig. 6).
†Operation by transthoracic route; all others done through the abdominal approach.

CASE REPORTS

CASE 1.—M. B., a white woman, 21 years of age, entered the hospital on Dec. 14, 1943, because of dysphagia, loss of weight, weakness, fainting, and dysmenorrhea. She had had dysphagia since the age of 11 years, which had become much worse during the past years. General physical examination at this time was essentially negative. Hemoglobin was 86 per cent and the red count 4,330,000. The total protein in the blood was 6.37 mg. per 100 c.c. of blood, the albumin 4.34, and the globulin 2.03. The blood Wassermann test and urinalysis were negative. X-ray studies showed a tortuous esophagus, greatly dilated, containing much retained food and fluid (see Fig. 7, *A* and *B*). Esophagoscopy on December 15 showed the esophagus to be ballooned out into a huge thin-walled structure, containing 2,000 c.c. of semi-digested food and debris. The esophageal wall was so thin that the right side of the heart could be seen, permitting observation of rhythmic or individual movements of the ventricle and the auricle. A No. 16 bougie passed through the cardiac orifice into the stomach without difficulty. There was no evidence of ulcer or tumor. The patient was placed on a clear liquid diet, was taught how to wash out the esophagus, and was discharged, to return to the hospital on Jan. 10, 1944, for operation. The general physical examination then was essentially the same as at the previous entrance. Esophagogastrostomy was done Jan. 13, 1944, through a transabdominal approach and a small piece of the cardiac ring was removed for study. The pathologist reported hyperplastic esophageal and atrophic gastric mucosa. This patient developed a slight wound infection and a pelvic abscess which was drained through the cul-de-sac. For the first five days she received nothing by mouth. By Feb. 6, 1944, when she was discharged, she was able to take a soft diet without difficulty. Her only comment was that she could feel the food go through the esophagus, drop directly into the stomach, and hit the posterior wall. She gained in weight, from 85 to 128 pounds. Since then she has gone through a normal pregnancy without difficulty. Roentgenograms taken in December, 1945, showed the esophagus still large, but no delay in emptying.

Fig. 1.—Exposure and freeing of lower end of esophagus.

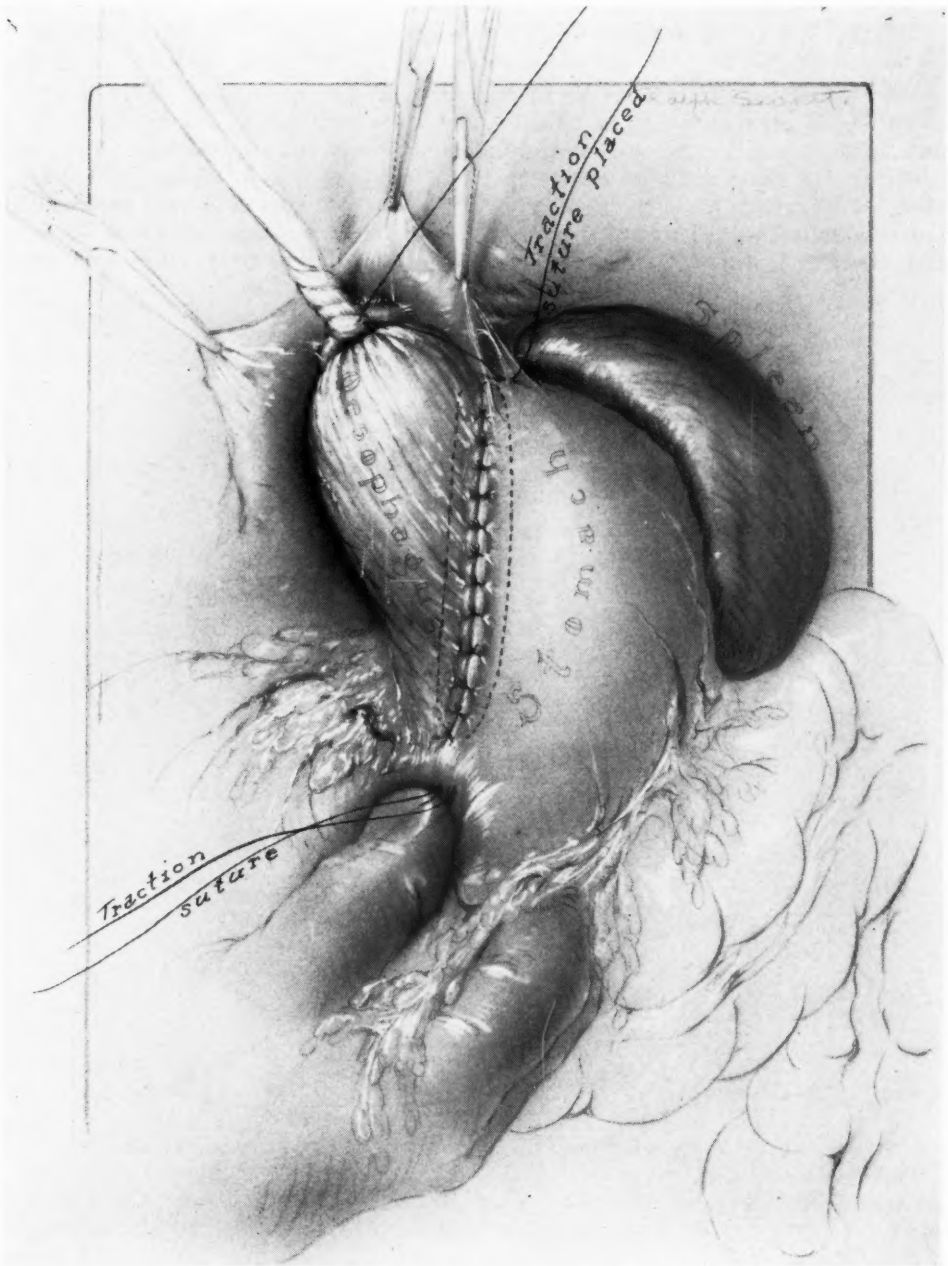


Fig. 2.—Posterior row of interrupted cotton sutures laid and tied; control of esophagus by cotton tape.

CASE 2.—F. T., a Mexican woman, 36 years of age, had had bouts of vomiting after taking food, either solid or liquid, for the past ten years. This might occur immediately or one and one-half hours after taking food. There was no blood in the vomitus. She had some slight epigastric pain radiating through to the back, which had become much worse during the last six months. Her normal weight of about 100 pounds had dropped to 68 pounds. She entered the hospital on Dec. 28, 1943, and was discharged on Jan. 30, 1944. General physical examination showed a markedly cachectic young woman. Blood pressure was 110/70; the hemoglobin was 95 per cent, red count 3,830,000, and white count 4,350. The urinalysis was essentially negative except for from 10 to 15 white blood cells and some bacteria. The phenolsulfonphthalein test was 72 per cent. The total blood protein was 5.95 mg. per 100 c.c. of blood, the albumin 2.79, and the globulin 3.16. The blood Wasermann test was negative. The x-ray studies and an esophagoscopy showed a hugely dilated esophagus filled with debris and fluid (see Fig. 8, *A* and *B*). Several transfusions of blood were given and an esophagogas-

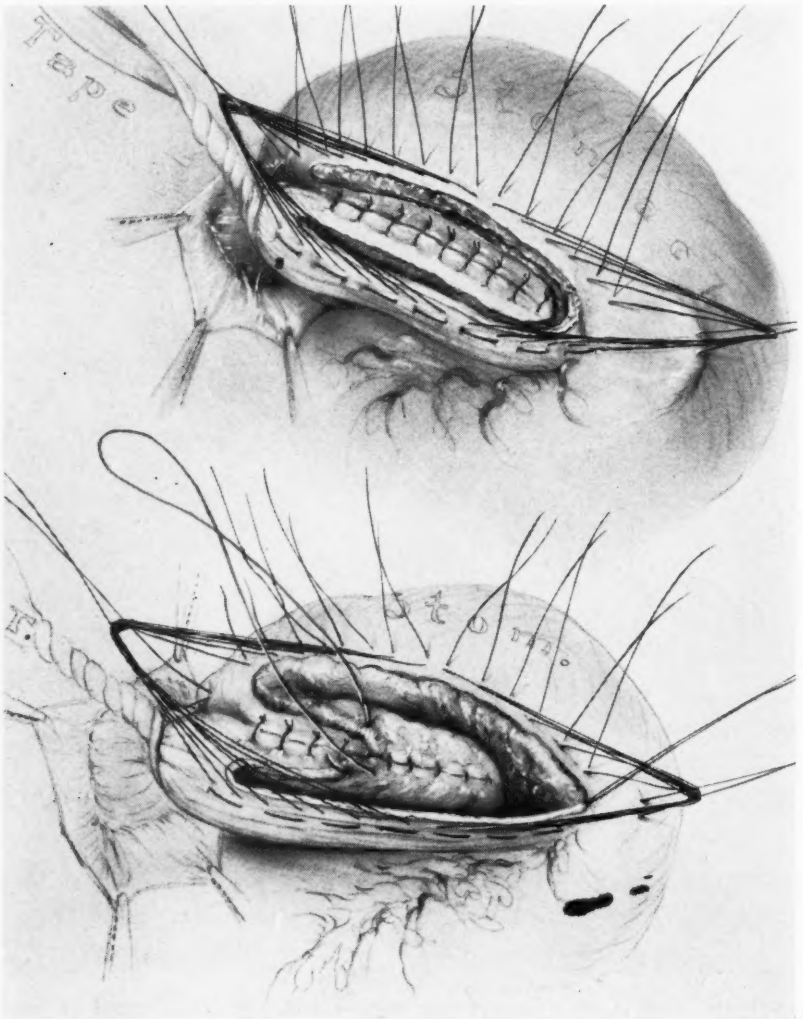


Fig. 3.—Posterior sutures tied. Anterior mattress sutures laid and retracted over traction sutures. Opening made in stomach and esophagus through the cardiac ring. Upper traction suture through stomach and cotton tape. Second posterior row of continuous 0000 chromic catgut sutures being placed.

trostomy was performed on Jan. 15, 1944. The course was uneventful after operation. The patient was pregnant at the time and subsequently had a full-term delivery of a normal child. Her weight increased to 118 pounds.

This patient re-entered the hospital on Dec. 11, 1944, because of some epigastric distress, weakness, and marked secondary anemia apparently resulting from a duodenal ulcer or ulcer at the anastomosis. X-ray studies showed the esophagus still to be somewhat dilated, but much smaller than it was at the time of the examination before operation. The barium went through without difficulty. The hemoglobin was built up from 28 to 75 per cent on discharge.

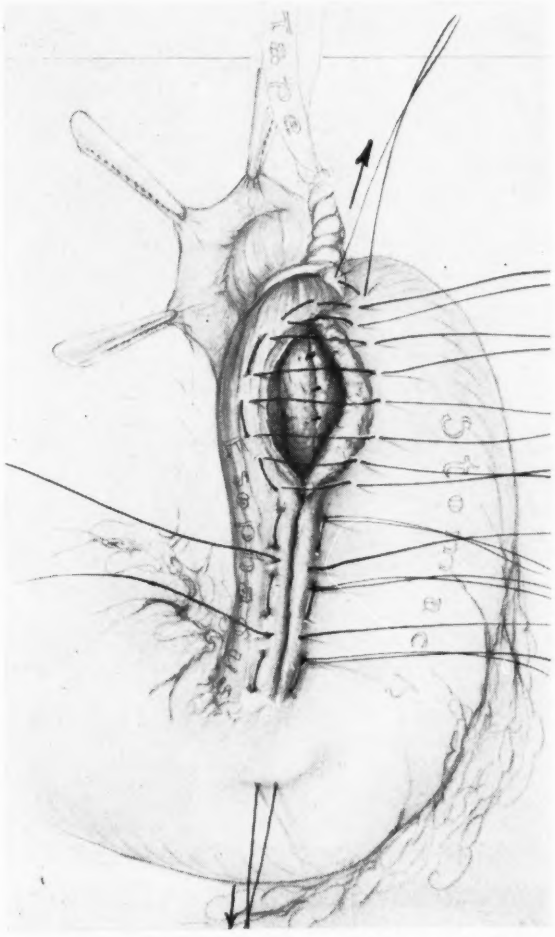


Fig. 4.—Anterior sutures being tied; interrupted Lembert sutures between each mattress.

CASE 3.—A. S., a white woman, 54 years of age, entered the hospital on April 27, 1944, because of vomiting for three weeks. History showed that she had had episodes of vomiting for twelve years, the attacks usually occurring immediately after breakfast. She always had had some difficulty in swallowing. X-ray studies and esophagoscopy showed a markedly dilated esophagus filled with liquid and food. Examination of the blood showed the hemoglobin to be 92 per cent, the red count 4,800,000, and the white count 6,650. Urinalysis and the blood Wassermann test were negative. An esophagogastrostomy was done on May 20, 1944. Since operation the patient has been well except when she becomes upset. At such times she forces herself to vomit. She is under observation for a pelvic condition unrelated to the chief com-

plaint and, at the time of her last entry, she complained that she vomited everything and was unable to swallow food, yet it was noted that she ate heartily, even asking for three extra helpings, and that she retained the food well except when members of her family were present. X-ray studies showed the esophagus to be somewhat dilated, although not so much so as before operation, and the barium went through without delay.

Fig. 5.—Completed operation; esophagus being fastened to the diaphragm.

CASE 4.—J. M. L., a white man, 35 years of age, entered the hospital on March 30, 1944, and was discharged on April 17, 1944. His chief complaint was that, since the fall of 1941, he vomited whenever he drank beer or carbonated water. This started at the time he was obtaining a divorce. The vomiting occurred at no other time. It was associated with pain high in the epigastrium. The symptoms of regurgitation and vomiting became much worse during the period in which he was obtaining a divorce. In 1942 he joined the Navy and worked very long and arduous hours. He would awaken at night to find regurgitated food on his pillow. On several occasions he was in Naval hospitals, where a dilated esophagus was demonstrated by x-ray examinations and esophagoscopies. Antispasmodics were administered and dilatation was done. He was finally discharged from the Navy in August, 1943. His weight had dropped from 155 to 136 pounds. After discharge from the Navy the vomiting and dysphagia increased. X-ray studies showed that about 50 per cent of the barium remained in the esophagus after six hours. The lower end of the esophagus came to a very fine point. The general physical examination on entry was entirely negative. Examination of the blood showed 94 per cent

hemoglobin with a red cell count of 4,790,000 and a white count of 5,200; the protein content was 5.59 mg. per 100 c.c. of blood, the albumin 3.98, and the globulin 1.61. The blood Wassermann test was negative. An esophagogastrostomy was done on April 6, 1944. The postoperative course was entirely uneventful and he was discharged twelve days after operation. His present weight is 150 pounds; he holds a very responsible position, can eat anything, and has had no more vomiting.

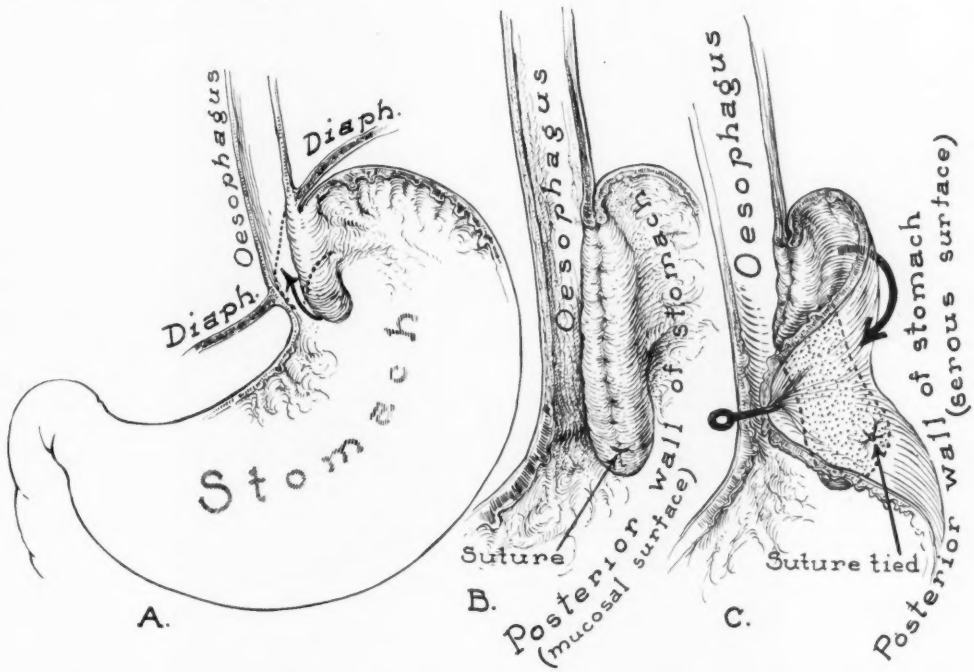
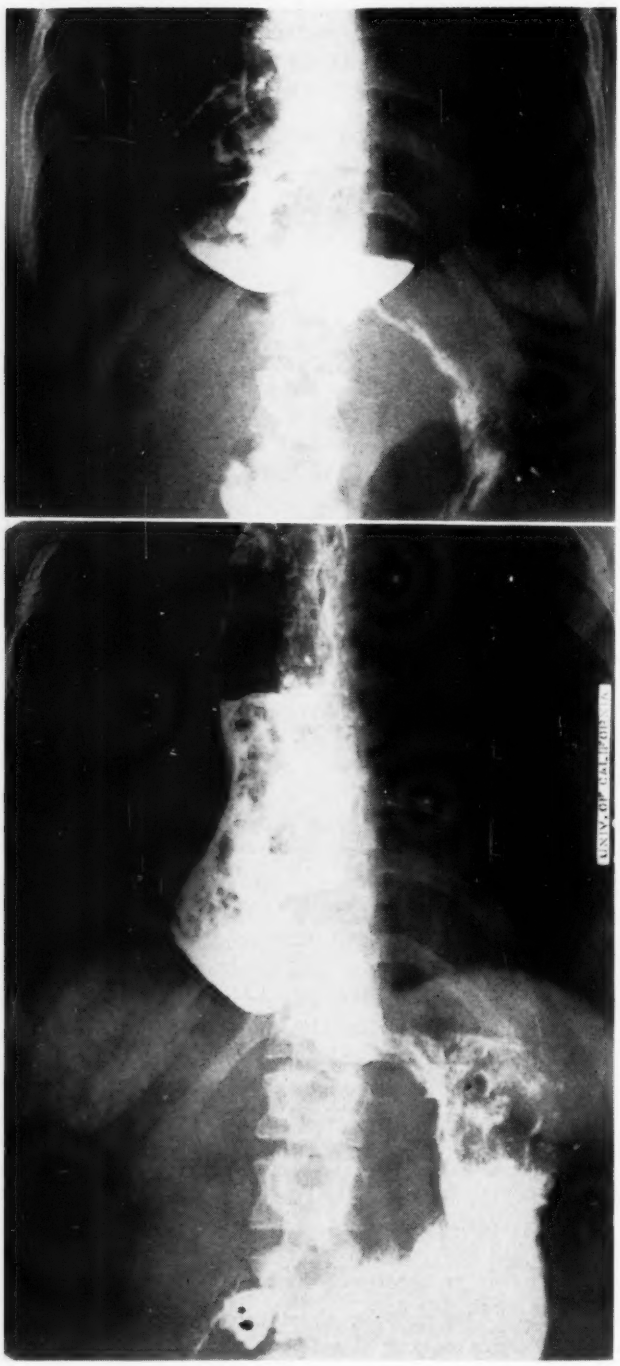


Fig. 6.—Showing flaplike valve action of posterior wall in two patients and method of correcting it. One suture placed through the flap and through the stomach wall and tied on the posterior wall.

CASE 5.—D. S., a white woman, 74 years of age, entered the hospital on Oct. 5, 1944, and was discharged on Oct. 24, 1944. The chief complaint was that for two years she had had difficulty in retaining food. At first she had trouble only with solids, then with soft foods, and finally with liquids. She had lost fifty pounds in weight. No pain was associated with swallowing. This patient had been studied elsewhere and an exploration of the abdomen had been done to rule out carcinoma of the cardia. She was not benefited by this operation. The hemoglobin was 74 per cent, the red count 4,000,000, and the white count 8,600; urinalysis was negative. The blood pressure was 170/80. X-ray study and esophagoscopy showed a widely dilated and tortuous esophagus. Esophagogastrostomy was done on Oct. 10, 1944. The postoperative course was uneventful and she was discharged on the fourteenth postoperative day. Microscopic study of the tissue removed from the cardiac ring showed a chronic inflammation and fibrosis. This patient has done very well since operation and has gained twelve pounds in weight. She has had no vomiting except after some unusual mental strain such as an argument with friends or relatives. Occasionally she has regurgitation if she stoops over quickly soon after a meal.

CASE 6.—G. R., a white man, 53 years of age, entered the hospital on Sept. 24, 1944, and was discharged on Oct. 14, 1944. He had had difficulty in swallowing for four years and recently had become worse so that he began to lose weight. He had no real dysphagia but did have to drink large quantities of water in order to be able to swallow soft food. He had had repeated dilatations and x-ray studies during the four years and antispasmodics had been

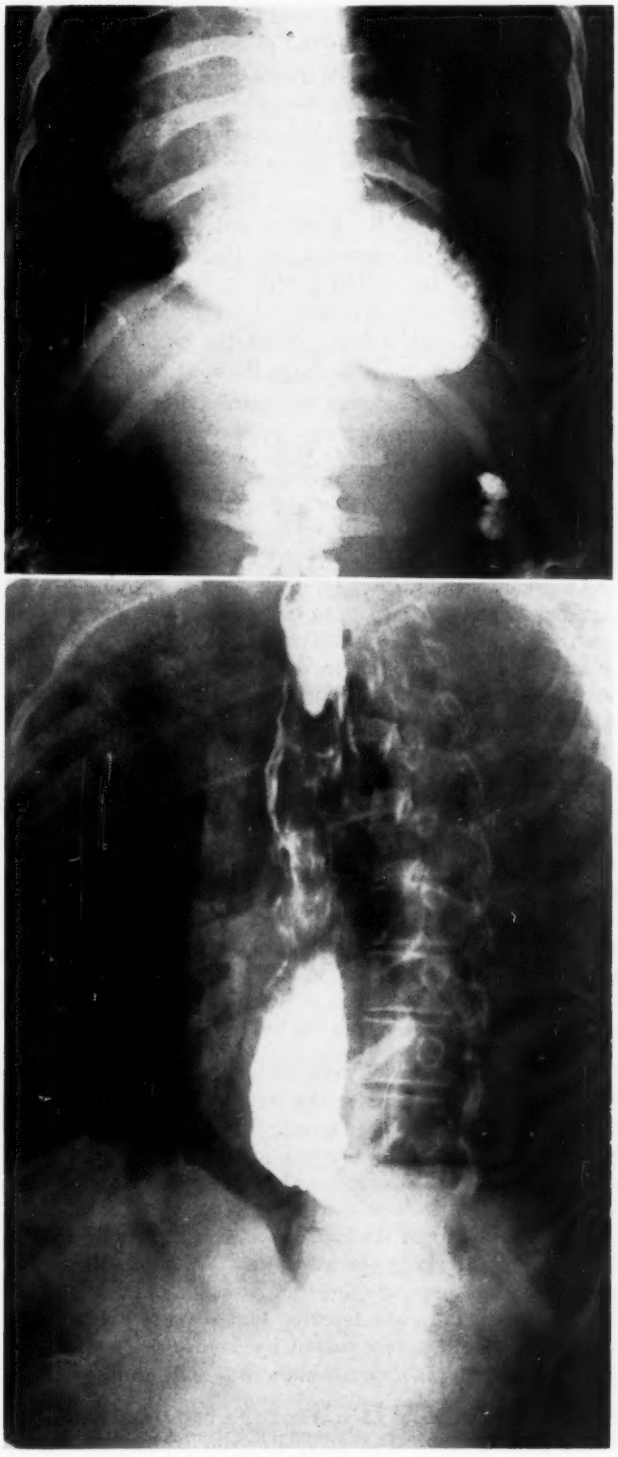
A.



B.

Fig. 7 (Case 1).—*A*, Roentgenogram taken before surgery. *B*, Roentgenogram taken after surgery.

A.



B.

Fig. 8 (Case 2).—*A*, Roentgenogram taken before surgery. *B*, Roentgenogram taken after surgery.

tried. X-ray studies and an esophagoscopy showed a dilated esophagus with the sigmoid curve to the right at the lower end of the esophagus near the cardiac orifice. No ulcer or tumor was seen. He had lost ten pounds in weight but the general physical examination was otherwise negative. Blood pressure was 130/80. The Wassermann test was negative as was the urinalysis. Examination of the blood showed the hemoglobin to be 94 per cent, the red count 4,640,000 and the white count 5,400. An esophagogastrostomy was done on Oct. 2, 1944. The postoperative course was uneventful but, as far as the ability to swallow was concerned, improvement was slight.

On Dec. 1, 1944, he returned to the hospital and an esophagoscopy was done. There was no evidence of ulceration, but it appeared that the new opening was not as large as it should be. Also, it showed that the posterior wall of the anastomosis acted like a flapper valve. A No. 16 bougie went through the orifice without difficulty. Thereafter the patient improved somewhat and regained some weight. Since the outcome could not be called satisfactory, a subsequent operative procedure to enlarge the opening was required.

Reoperation was done Jan. 30, 1945, and the opening was enlarged and the posterior wall of the anastomosis which acted like a valve was fastened to the posterior wall of the stomach (Fig. 6). Since then he has gained weight and has no difficulty in swallowing.

CASE 7.—E. M., a white woman, 61 years of age, entered the hospital on Oct. 17, 1944, and was discharged on Oct. 31, 1944. The complaint was of regurgitation of undigested food and liquids and some pain at the lower end of the xiphoid process. She dated the complaint from a time one and one-half years previously, when she fell, striking over the xiphoid process, and also fracturing some ribs. The vomiting gradually grew worse, particularly if she became mentally upset. Her weight dropped from 140 to 116 pounds. X-ray examinations and esophagoscopy showed marked dilatation of the esophagus without evidence of ulcer or tumor. The cardia was dilated with but temporary relief. General physical examination was negative except that the blood pressure was 185/100. Examination of the blood showed the hemoglobin to be 100 per cent, the red count was 5,120,000, and the white count and differential were normal. The blood Wassermann test and urinalysis were negative. An esophagogastrostomy was performed on Oct. 19, 1944. The postoperative recovery was entirely uneventful and she was discharged on the twelfth day after the operation. Microscopic examination of the tissue removed from the cardiac ring showed fibrosis and chronic inflammation, with edema. This patient did fairly well after operation but continued to have some difficulty in swallowing food, particularly following mental upset. From a surgical standpoint her condition was not entirely satisfactory.

The patient re-entered the hospital April 19, 1945, for reoperation. At operation the posterior wall of the anastomosis was found to be acting like a valve. It was sutured back to the posterior wall (see Fig. 6). Since then she has gained weight.

CASE 8.—M. L., a white woman, 37 years of age, entered the hospital on Nov. 29, 1941, and was discharged on Dec. 24, 1941. For the last two and one-half years she had vomited almost every day, particularly after taking water. She had a sense of fullness at the base of the esophagus directly over the xiphoid. She had lost some weight and suffered paroxysms of vomiting. In December, 1939, x-ray studies and esophagoscopy had shown a dilated esophagus. A general physical examination was essentially negative. The cardiac end of the esophagus was dilated on nine occasions, on the last of which a perforation at the lower end of the esophagus was caused. An emergency operation was performed, through a transthoracic approach, and an esophagogastrostomy was done on Nov. 29, 1941. The postoperative recovery was very good. In December, 1944, she reported that she was able to swallow perfectly, but had had recurrent attacks of biliousness caused by disease of the gall bladder. Apparently this illness had no connection with the operation on the esophagus.

CASE 9.—H. G. W., a white man, 65 years of age, entered the hospital Dec. 11, 1944, and was discharged Dec. 27, 1944. The chief complaint was that he was unable to eat any solid food for the last three months. He had lost ten pounds in weight.

Past history revealed that he had been in this hospital in October, 1935, because of regurgitation of food recently eaten, which had been going on for four years before that. The vomitus and regurgitation consisted of unchanged and undigested food. At times he would vomit food eaten twenty-four to forty-eight hours before. His weight dropped from 154 to 120 pounds. This episode of vomiting and regurgitation came on very shortly following the rather sudden death of his employer, of whom he was very fond. He noticed recurrence of severe attacks of vomiting when under an undue amount of emotional strain.

General physical examination at this entry was essentially negative. All the laboratory work was entirely within normal limits and the only positive findings were the x-ray findings of the esophagus. X-ray examination of the esophagus showed it to be a large, easily dilatable tube with very active peristalsis. At the lower end, just above the diaphragm, there was a marked, funnel-shaped narrowing of the esophagus.

An esophagogastrostomy was done Dec. 15, 1944. A biopsy of the cardiac ring was taken, and the pathologic report revealed tissue from the esophagus showing chronic inflammation and fibrosis. The postoperative course was essentially uneventful. He was discharged from the hospital twelve days postoperatively, taking a soft diet without difficulty.

CASE 10.—R. R., a colored woman, 27 years of age, entered the hospital Dec. 22, 1945, because of loss of weight, weakness, and vomiting after eating. This difficulty had been present for at least eleven months, and had become severe during the past six months. Her weight one year before was 176 pounds, and at the time of admission was 104. She thought the vomiting began after she had taken some pills prescribed for her by a chiropractor to bring on menstruation. After taking the pills for two days, a "blob of stuff" was ejected just like a miscarriage, and bleeding continued, off and on, for three weeks. She complained that the pills made her throat burn and contract down so that food would not go through. Following this, the burning sensation continued and she consulted a doctor who took roentgenograms and found a markedly dilated esophagus with a very narrow opening into the cardiac end of the stomach. These findings were confirmed at this hospital. She was found to have a 4 plus Wassermann reaction and she was put on an intensive course of antisyphilitic therapy. During this time, however, there was no change in the ability for her to keep food down. The general physical examination upon entrance into the hospital was essentially negative, except for evidence of weight loss. Blood pressure was 120/80, hemoglobin 92 per cent, red count 4,310,000, white count 7,200, with a normal differential. The urine was negative. Due to an extremely sensitive gag reflex and lack of cooperation of the patient, dilatation was not satisfactory. She was prepared in the hospital by washing the esophagus out twice a day for five days. Some of the material returned was very foul smelling. An esophagogastrostomy was done on Dec. 31, 1945. The postoperative course was very smooth. It is too short a time to give any particular follow-up on this patient.

DISCUSSION

Certain characteristics are evident in all of these cases. For example, the patient's symptoms become pronounced when he is under mental or emotional strain. When all facts are considered, it seems evident that some neurogenic factor enters into the etiology of the condition. This is especially evident in Cases 3, 4, 5, 7, and 8.

The ages varied widely, indicating that cardiospasm may be found at almost any age. In the small number of cases reported, the disease was more common in women than in men.

The results of esophagogastrostomy have proved so satisfactory in the ten patients treated by this method that the performance of the operation is felt to be justified. There were no deaths in this series, and eight patients received complete relief; two patients required a subsequent operation. Esophago-

gastrostomy appears to offer a more direct approach to the problem than any other of the numerous operations suggested. The details of the operation have been so well described by Ochsner and DeBakey[2] that further report other than the illustrations seemed unnecessary.

ADDENDUM

Dr. Clayton Lyons of our Staff has recently operated upon a sailor for severe cardiospasm through the transthoracic route with excellent results. This patient had had two previous procedures done through the abdomen for dilatation of the cardia without benefit.

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TRANSPLANTATION OF TOES FOR FINGERS

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THE purpose of this report is to consider the transplantation of toes as a means of repairing losses of fingers. The indications for replacing partially or completely lost fingers is for the most part cosmetic although to a certain extent utilitarian. One can get along well with three or even two fingers as long as the thumb is intact. However, a lost thumb constitutes a great disability and when possible some substitute should be furnished. For this reason most reported reconstructions of lost digits of the hand have been restorations, by one means or another, of the thumb. There are numerous methods which have been used more or less successfully. Among these are prosthesis, phalangization, rotary angulatory osteotomy, tubular pedicled graft with inserted bone graft, transplantation of index finger to position of thumb, and digital transplantation from either the hand or the foot. We will not discuss, in this report, the merits or objections to the various methods used in thumb restoration.

If one wishes to replace a lost finger, only a few of these are applicable. Prosthesis is mentioned only to be discarded. While a prosthesis may perform a fair cosmetic function if carefully made and colored, it is insensitive, troublesome to keep on, and is usually soon given up by the wearer. A finger can be elongated to normal by a tubed graft of skin and subcutaneous tissue into which a bone graft is later inserted and fixed to the metacarpal or the most distal phalanx present. Such a substitute fails cosmetically since the skin is neither the same color nor texture, and does not have a nail. The transplantation of a toe comes closest to fulfilling requirements of appearance and function.

The substitution of toes for fingers was first conceived by Nicoladoni.[1] He reported, in 1900, the substitution of a part of the second toe for a partial defect of the thumb. The method has become known as the Nicoladoni procedure, although Von Eiselsberg[2] in the same year reported the transplantation of the second toe to replace an almost complete loss of the index finger.

Since then there have been scattered reports on the subject. In 1930 Gueullette[4] collected 20 cases of reconstruction of the thumb by digital transplantation. He found 12 cases in which the great toe had been used, 5 in which the second toe was used, and 3 in which a finger had been transplanted. Of these 20 cases, 7 had active movement and there were only 3 which he classified as perfect.

Bunnell,[19] in discussing the subject of reconstruction of the thumb, more or less condemned digital transplantation. He stated, "The transplanted digit undergoes atrophy as in a paralytic finger or one with a girdling scar, all its

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tissues suffering. Sensation is very poor, as no one as yet has reported reconnecting the nerves. Trophic sores and deep, progressing ulceration have occurred. In most cases the new digit is hooked, atrophic, stiff, and without motion.'' By inference one is led to believe that he favors other methods of reconstructing the thumb.

However, from the more recent literature one is not inclined to look upon the matter in quite such a pessimistic light. There are some results which have been examined and reported years afterward which appear to have been quite worth while and most of the poor ones can, I believe, be attributed to technical difficulties or to poorly conceived substitutes.

For example, Oehlecker[11] reported a twenty-year follow-up on a case in which the great toe was transplanted to replace a left thumb lost at the metacarpophalangeal joint. The patient was a chemistry professor, was able to hold test tubes, beakers, etc., with the thumb and index finger, played the violin, and was completely satisfied with the digit.

Ranschburg[16] reported the neurologic findings twenty years after Esser had transplanted part of the metacarpals and four small toes to a hand on which only the thumb was present. In this case the tendons had been united. The man was able to flex the toes and hand in mass to oppose the thumb. The neurologic findings twenty years later were most interesting. Light touch was excellent. Localization of touch on the volar surface was good, the man being able to localize which finger-toe was touched, but on the dorsum knew only that the dorsum rather than the volar surface was stroked. He could localize pain stimuli correctly. Temperature sense on the transplanted foot-hand was far more accurate than on the normal foot. There were four to five times as many false answers to temperature tests on the normal foot as on the transplanted one. This man was able to use the hand in farm work and got along satisfactorily.

A somewhat less satisfactory result was reported by Neuhof.[18] The difficulty in this case which was reported seventeen years after the transplantation can be attributed, I believe, to the fact that a toe cannot be expected to grow to the size of a finger; this illustrates that some cases classified as unsatisfactory are due to errors in the original conception of the substitution. When the patient was 7 years of age, the second toe was substituted for a complete congenital absence of a middle finger. The toe slowly increased in length and thickness until adult life; but remained more nearly the length of a toe than a finger. Neuhof stated that sensation returned in ringlike fashion and was ''normal'' in about six months.

During the past ten years we have found twelve reports on this subject. It is interesting to note that six of these have come from Soviet Russia where the operation seems to have been more used than elsewhere. For the most part these transplantations have been successfully accomplished and the ultimate result has been worth while.

From the literature one gains the impression that for losses of the thumb from the metacarpophalangeal joint distally, transplantation of the great toe

on the *opposite* side is the best digit for substitution. This is so because the position of the hand on the opposite foot is a natural one that can be maintained without strain. Finger reconstructions should be limited to losses which are such that the transplanted toe can restore normal length. The best digit for substitution is the second toe on the same side. One further notes that the almost sole cause of failure is the inability of the patient to bear the irksome position for the necessary period of three to four weeks. If the pedicle is divided too soon, the toe is lost completely or has a period of poor circulation which later predisposes to atrophic changes and scarring. It is also evident from the various reports that, even though the tendons be united, active motion is not assured. However, in practically all instances fair sensation returns in ring-like fashion from the anastomosis to the distal tip. The return of touch pain, and temperature is constant. Localization of touch is fair but astereognosis is the rule.

OPERATIVE PROCEDURE

The operation reported in most instances varies little from the original Nicoladoni procedure. The details may differ depending upon the level of the finger loss.

A U-shaped skin flap is turned distally at the base of the second toe and both dorsal arteries are divided. The extensor tendon of the toe is cut high, the periosteum reflected as a cuff, and the bone divided. A transverse incision is made across the stump of the finger, the extensor tendon located, the periosteum reflected from the bone, and the bone end freshened. The distal end of the sectioned bone of the toe is dislocated and the bone of the finger and toe approximated by suturing the reflected periosteal cuffs. The extensor tendons are sutured so that the suture line is proximal to the periosteal closure. The skin flap is sutured to the skin of the finger and a plaster cast applied. In about one month the volar attachment is divided and the flexor tendons are sutured.

In the case to be reported, the operation was modified in two respects. First, the incision on the toe was made longitudinally down to the extensor tendon and the tendon sectioned. Thus, the entire arterial supply of the toe was preserved. Second, since the distal two phalanges of the second toe corresponded exactly in length to the amount of finger lost, the proximal phalanx was dissected out subperiosteally and removed, leaving the joint capsule of the proximal interphalangeal joint attached to the proximal end of the second phalanx. The flexor tendon of the toe was then severed. A dorsal triangular shaped skin flap was raised from the stump of the finger. The capsular periosteal structures were elevated as a cuff from the phalanx and the extensor and flexor tendons isolated. The end of the phalanx, which was covered by fibrous tissue, was then inserted into the trough made by removal of the proximal toe phalanx, and the joint surfaces approximated by suturing the reflected capsular cuffs and the flexor and extensor tendons. The triangular finger flap of skin was sutured to the edges of the longitudinal incision on the dorsum of the toe. The necessary position had gradually been gained prior to operation, and

all that remained to be done was immobilization of the arm to the flexed lower extremity. The details of the case are as follows:

CASE REPORT

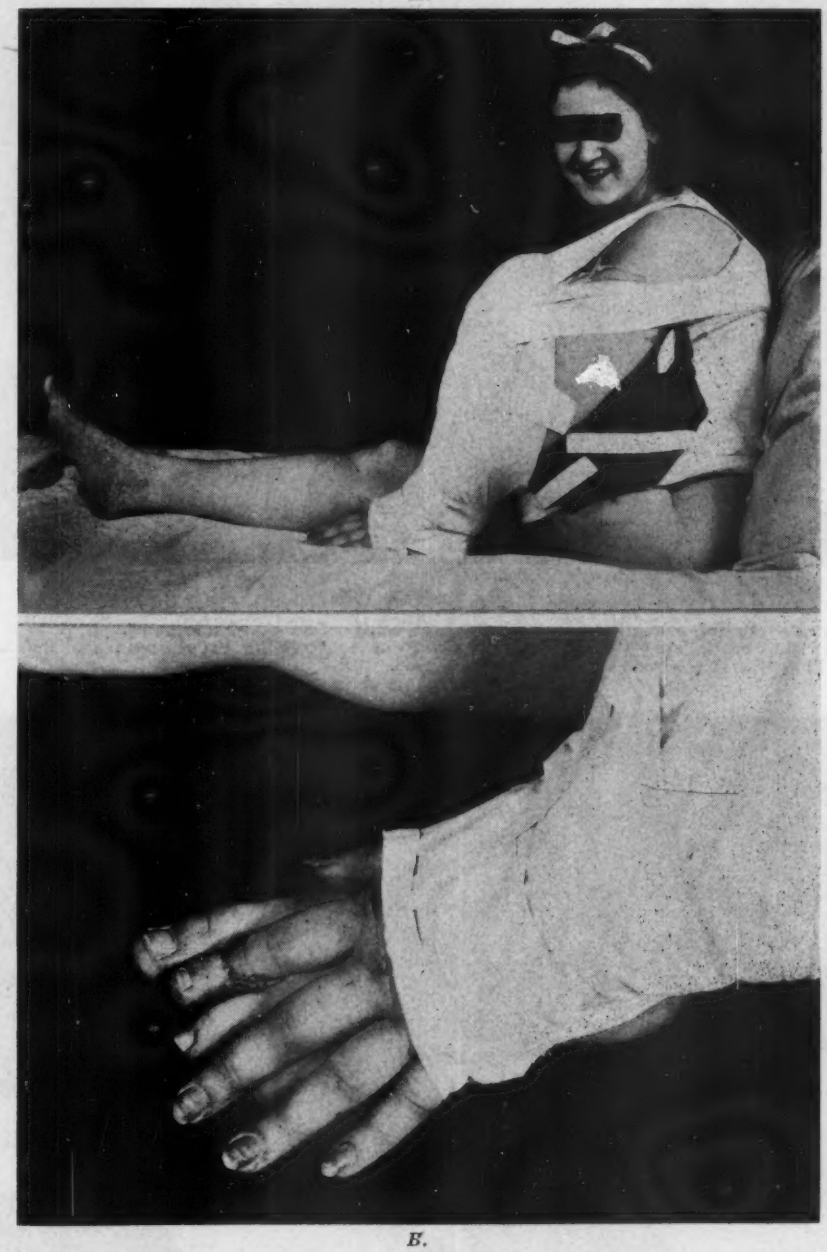
G. M. (S. M. H. No. 227476), a 26-year-old, single white woman, a stenographer, was first seen Jan. 17, 1945, because of a partial amputation of the left index finger. On Dec. 12, 1944, she was attempting to disengage the locked bumpers of two cars. The driver of one car was her sister, who inadvertently put the car in gear, catching the patient's left index finger between the bumpers. The finger was amputated at the mid-portion of the middle phalanx. When seen six weeks later the stump was well healed (Fig. 1). There was considerable anxiety on the part of the sister, who felt responsible and wished everything possible done to repair the damage. They were advised that a toe transplant could be done after the injured finger had returned to a more normal state.

Fig. 1.—Loss of index finger just proximal to the distal phalangeal joint.

The patient was admitted to the Strong Memorial Hospital on April 25, 1945. On April 28 the left knee was immobilized in acute flexion in a plaster cast. The circulation of the foot remained satisfactory and four days later a body cast was applied to hold the left hip in acute flexion. The patient tolerated the position well and four days later, on May 5, 1945, the stump of the left index finger was attached to the left second toe as described (Fig. 2). The side of the cast was padded with felt and the arm was immobilized against it with elastic adhesive. The wound healed cleanly. The circulation of the toe remained completely normal. The patient tolerated the position exceedingly well. On May 27, 1945, twenty-two days later, the toe pedicle was divided from midline dorsally to midline volarly, vessels were ligated, and the wound was sutured. The circulation remained completely normal. On June 5, 1945, exactly one month after attachment, the pedicle was completely severed. No attempt was made to suture the wound as it was feared this might compromise the blood supply. The wound smoothed out spontaneously and quickly healed. The patient was discharged from the hospital on June 14, 1945. On Oct. 8, 1945, she was re-admitted to the hospital and the excess soft tissue at the junction trimmed out on one side (Fig. 3). It is planned to do this on the remaining side, but since the patient married and became pregnant, this has been delayed. She was last seen on Jan. 26, 1946, about eight months after completion of the transplant and only about three and one-half months since the trimming operation. The finger is normal color and the nail has already become more fingerlike. There is no active

motion of the distal phalangeal joint (Fig. 4). Sensation has returned to the level of the nail bed. She is able to localize light touch and pinprick correctly over this area and to differentiate hot and cold.

A.

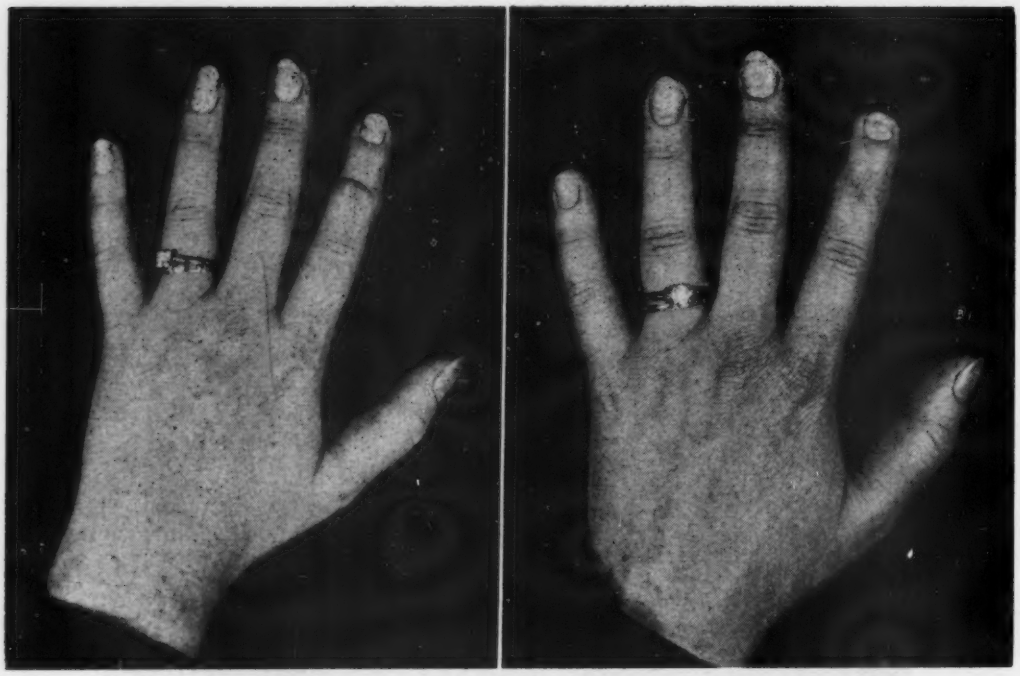


B.

Fig. 2.—*A*, This position was obtained gradually. The knee was first immobilized in acute flexion and after four days the trunk was encased in plaster and attached to the leg cast to hold the hip acutely flexed. If the patient tolerates these steps preoperatively, the chances of maintaining the position for the necessary four weeks are good. *B*, The circulation of the toe remained normal and the finger and toe healed together cleanly.

SUMMARY

The transplantation of a toe to replace a missing digit of the hand was first reported by Nicoladoni in 1900. There are now a few cases in the literature which have been followed for as long as twenty years. From these reports it



A. *B.*

Fig. 3.—*A*, The soft tissues are redundant at the line of anastomosis. *B*, A few months later, one side of the finger has been smoothed out by excising excess skin and subcutaneous tissue. This will be repeated on the opposite side.

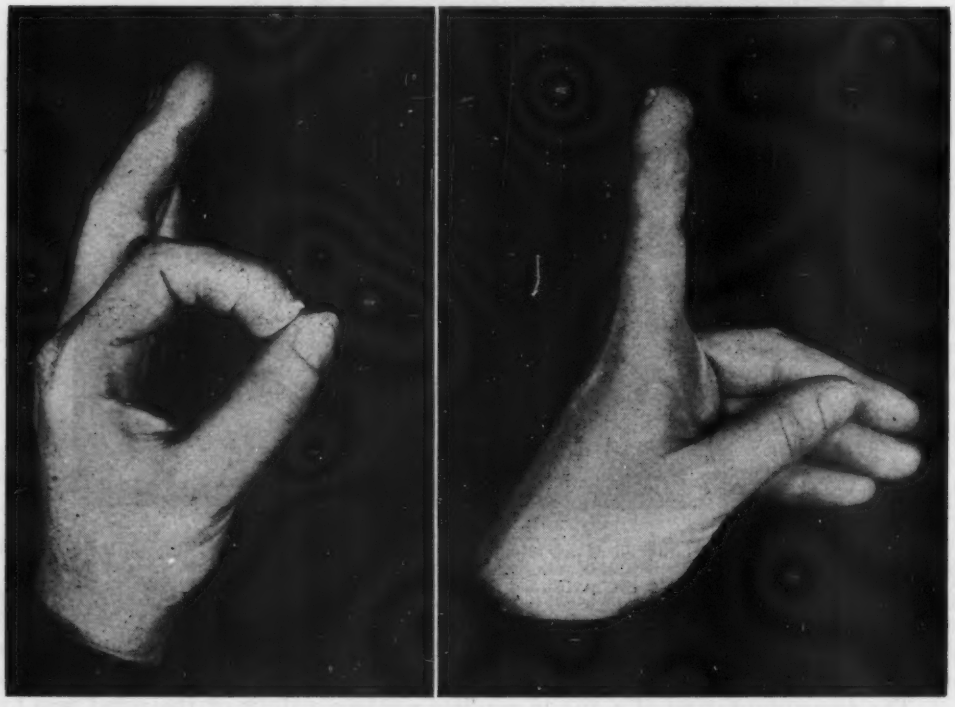


Fig. 4.—The finger is stable but has no active motion. Sensation has returned to the level of the nail bed. The finger can be usefully apposed to the thumb.

would seem that the ultimate result, while not perfect, is worth while. It has been found that replacement of the thumb is best done by transplanting the great toe of the opposite foot and that the second toe on the same side is most useful for finger restorations. Complete active motion of the transplanted digit is the exception rather than the rule, but sensation returns over a period of months so that localization of touch, pain, and temperature is fairly normal.

The replacement of a finger with the second toe is best limited to those cases in which the loss is such that the toe transplant can restore full length.

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CLINICAL AND EXPERIMENTAL OBSERVATIONS ON THE USE OF GELATIN SPONGE OR FOAM

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OF THE recent advances in operative surgical technique, the development of absorbable hemostatic agents is one of the most interesting. The success of fibrin foam in neurosurgery has been made possible by the plasma fractionation program which has been conducted in the department of physical chemistry of the Harvard Medical School[1] and by the experimental and clinical work on this material by Ingraham and Bailey,[2] and by Woodhall.[3] The usefulness of oxidizied or soluble cellulose has been well presented in several reports by Frantz and co-workers,[4] and others.[5]

A third hemostatic substance is gelatin sponge or foam. This was first described by Correll and Wise,[6] and subsequently has been the subject of excellent experimental and clinical evaluation in neurosurgery by Pilcher and Meacham,[7] and by Light and Prentice.[8] We have reported studies on the absorbability of gelatin sponge.[9] It was found to undergo absorption within about five weeks when implanted in the liver, kidneys, spleen, omentum, or abdominal wall. In the presence of a conspicuous leucocytic reaction the absorption was considerably accelerated. The response to the gelatin sponge was generally of a nature which could be described as a nominal or minimal tissue reaction as compared with what one frequently observes with absorbable suture material. Subsequent to the absorption there was no residual inflammatory reaction observed. A limited number of clinical observations were also reported. To evaluate the usefulness of the gelatin sponge in the hemostasis problems of general surgery, further experimental and clinical studies have been conducted.

A series of thirty dogs was subjected to laparotomy using aseptic technique and ether anesthesia. Wounds of various sizes and types were made in the liver, kidneys, or spleen. The gelatin sponge was moistened in saline solution, the air removed from the sponge, and the excess saline solution expressed from the sponge. It was then applied to the bleeding wound with gentle pressure for about three minutes. The sponge became adherent to the raw surface and controlled the bleeding. In a few instances a second application was necessary. No suturing was required to supplement the hemostasis or hold the sponge in place. The size of the wounds varied from a deep scalpel incision to a moderate-sized wedge-shaped resection of a portion of a lobe of the liver (see Fig. 1). In a few instances an entire lobe was removed. One of the most

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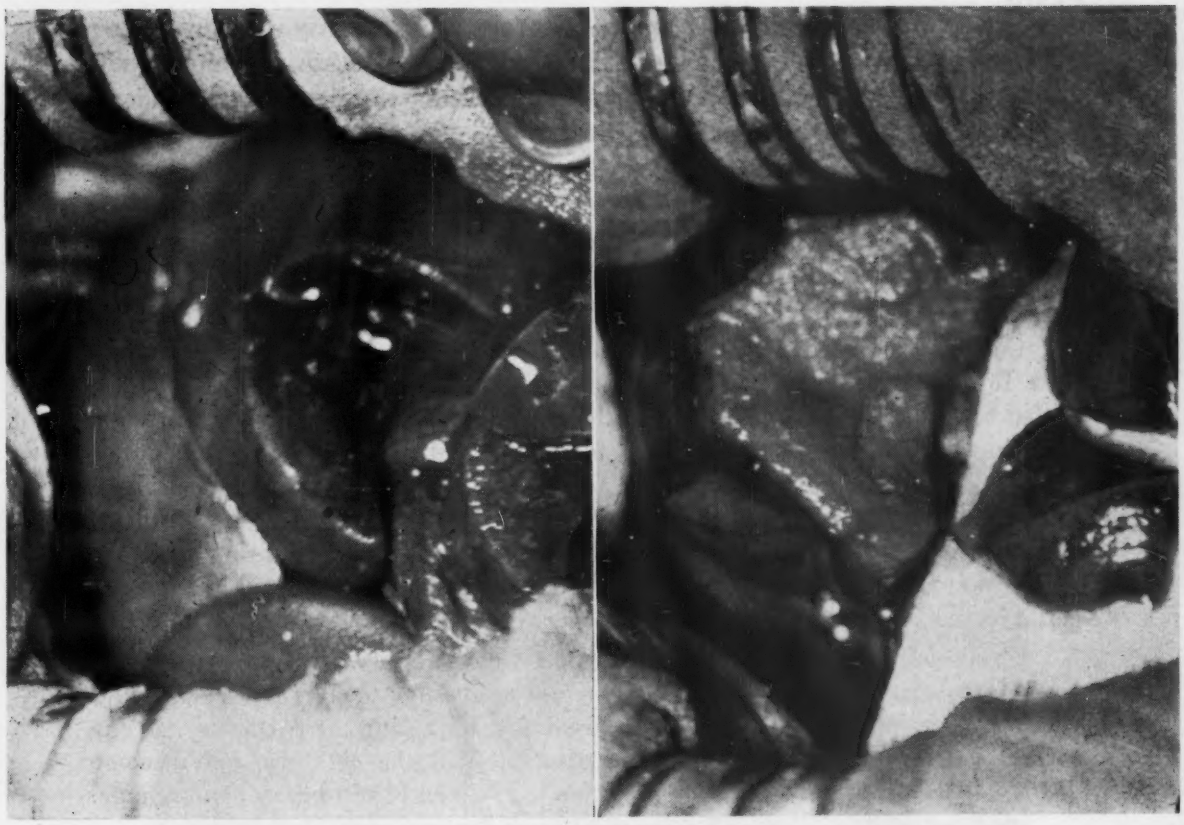

A. Fig. 1. *B.*

Fig. 1.—*A*, Wedge-shaped resection of liver tissue in experimental animal; free bleeding occurs from the raw surface. *B*, Gelatin sponge packed into the wound of the liver producing complete hemostasis. The sponge becomes rather firmly adherent to the raw surface of the liver. Liver tissue which has been resected is shown on gauze at lower portion of photograph.

Fig. 2.

Fig. 2.—Gelatin sponge (*A*), soluble cellulose (*B*), and fibrin foam (*C*) packed into wedge-shaped wounds of liver of experimental animal. Note the black appearance of the soluble cellulose. The hemostatic action of these three materials appeared to be about the same.

interesting observations aside from the control of the bleeding was the manner in which the sponge became adherent to the wound. Within one-half hour it would become sufficiently adherent to the raw surface that it was often difficult to remove the sponge without tearing it.

These experiments on the hemostatic action of the gelatin sponge were done for the most part without the addition of thrombin. In such experiments as were conducted with the gelatin sponge soaked in thrombin there appeared to be a more rapid hemostatic action, although this was not outstanding as compared with the sponge alone.

Control studies were made in many of the animals using soluble cellulose. In a few animals fibrin foam was also used (see Fig. 2). Thrombin was not added to either of these two hemostatic materials. The size or type of incision used in the liver, kidney, or spleen for these control studies was, of course, identical. The immediate hemostatic action of gelatin sponge, soluble cellulose, and fibrin foam appeared to be approximately the same. The soluble cellulose, which turns black upon contact with blood, did not adhere quite as firmly to the raw surface of the wound as the gelatin sponge. The fibrin foam mass could be more easily broken up than the gelatin sponge.

These animals were sacrificed at varying periods of time from one day to six months after operation. No evidence of secondary hemorrhage was found where the gelatin sponge had been used for obtaining hemostasis. In one animal, however, there was evidence that the soluble cellulose had become dislodged from a wound in the liver which led to a fatal secondary hemorrhage.

Within a few days the omentum was generally found to be adherent to the wounds packed with the hemostatic materials, thus forming a protective covering to the wound. In some instances there were adhesions to adjacent organs which were dependent to a considerable extent on the magnitude of the wound and the amount of hemostatic substance used. After about four days it was difficult to identify the soluble cellulose grossly although the gelatin sponge could generally be identified. In a few instances the gelatin sponge implanted in large wedge-shaped resections of the liver produced a small cavity within about ten days, which was walled off by adhesions to surrounding organs and the omentum, and which contained a rather gelatinous-like exudate. This undoubtedly represented the liquefaction of the gelatin sponge, since it could not be otherwise identified in the wound.

In these experiments where large wounds were made in the liver and other organs and large pieces or sponge implanted therein, it was generally found that the absorption of the gelatin sponge was more rapid than was observed in the previously reported study where relatively small incisions and small amounts of sponge were used. Microscopic studies of the tissues in this series demonstrated complete absorption of the gelatin sponge in a number of instances within two to three weeks. In the previous study there was microscopic evidence of the gelatin sponge in the liver up to thirty-four days.

A clinical evaluation of gelatin sponge has been carried out on sixty patients. In twelve cholecystectomies the sponge was used on the undersurface

of the liver to control the bleeding after removal of the gall bladder. It was necessary to hold the sponge in place with sutures in several of these. In five exploratory laparotomies at which a biopsy of the liver was taken, the sponge was packed into the bleeding wound in the liver and held in place by a few mattress sutures. In one of these cases two attempts were made to control the bleeding by packing with soluble cellulose for three minutes each. The bleeding was not controlled by the cellulose but after the application of gelatin sponge it promptly stopped. Three of these gelatin sponge implants in biopsy incisions in the liver, which were performed to establish the diagnosis of an inoperable neoplasm of the liver, were subsequently recovered at autopsy. The microscopic sections showed that the sponge was undergoing absorption in a manner similar to that which was previously described for the experimental implants in the liver (see Fig. 3).

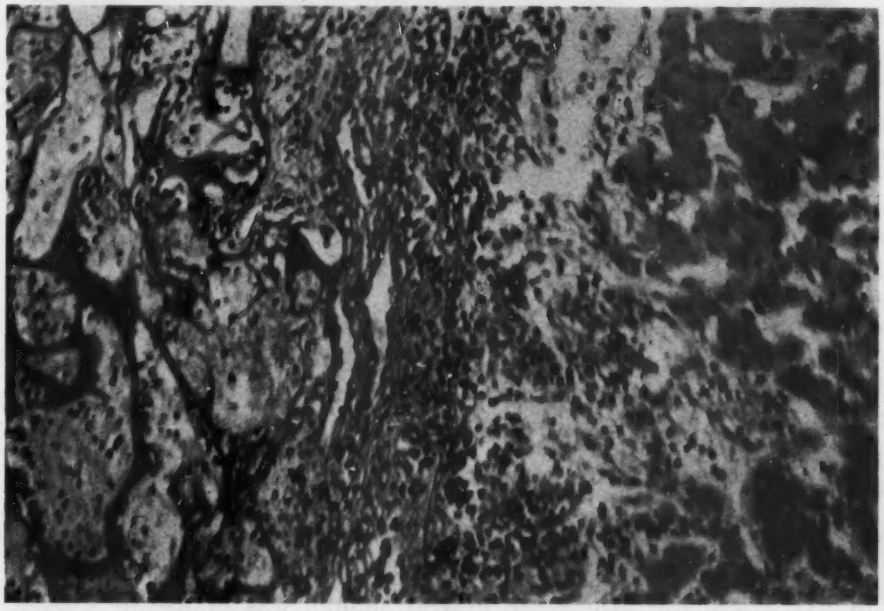

Fig. 3.—Photomicrograph of gelatin sponge in liver of patient seven days after exploratory laparotomy and biopsy of liver. Specimen was recovered at autopsy which demonstrated carcinomatosis and cirrhosis of liver. The interstices of the sponge are filled with red blood cells, some fibrinous exudate, and a moderate number of polymorphonuclear leucocytes. There is a zone of fibrosis and cellular invasion between the liver cells and the sponge.

In a splenectomy some very troublesome bleeding occurred from the undersurface of the diaphragm to which the spleen had been adherent. This bleeding was promptly controlled by the application of several large squares of gelatin sponge. It is believed that this contributed to the recovery of the patient. In two neoplasms involving the mesentery of the small intestine a biopsy was taken and rather troublesome bleeding encountered. This was controlled by the application of gelatin sponge.

In operations on the thyroid the gelatin sponge has been used in six thyroidectomies and in one biopsy (see Fig. 4). The magnitude of residual bleeding after ligature was relatively slight and ordinarily would not have required

additional ligature. Such slight oozing as was present was controlled by the sponge. In these cases there appeared to be somewhat more serum accumulation in the wound. In one of the patients there was extrusion of catgut knots for about one month after operation.

In three operations on the breast the gelatin sponge was especially useful for controlling oozing from the breast tissue after biopsy or removal of benign tumors. Some mattress sutures were required to hold the sponge in place. In one case the gelatin sponge was used after removal of a large fibroadenoma to fill in a dead space which would otherwise have produced a marked depression of the breast.

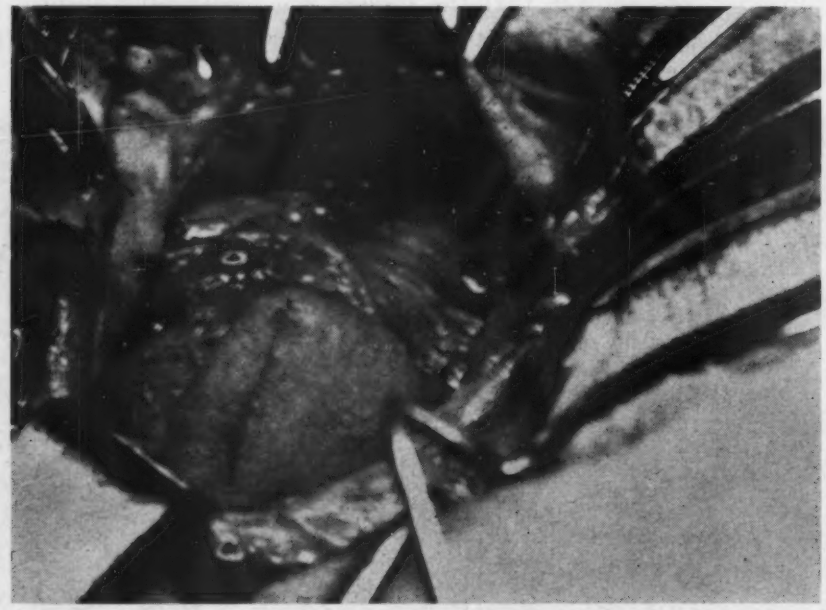

Fig. 4.—Gelatin sponge packed into biopsy wound of thyroid. This controlled the bleeding from the wound. As a precaution the sponge was held in place by several mattress sutures. (The diagnosis proved to be struma lymphomatosa.)

In five rectal operations the gelatin sponge was of use as a pack after hemorrhoidectomy, fistula operations, and an anal plastic for imperforate anus. The sponge is apparently rapidly liquefied in the rectum and eliminates the necessity for removing the usual type of pack which is seldom a comfortable procedure for the patient, and which may sometimes be inadvertently overlooked. We would like to mention one experience with soluble cellulose as a rectal pack after hemorrhoidectomy. On examination the following day, it was found to have formed an airtight plug which had the consistency of dried glue. It was dislodged from the rectum with some discomfort to the patient. We are inclined to believe that this is one place where soluble cellulose is most definitely contraindicated.

The gelatin sponge was used on dermatome donor areas in nine cases. It stopped the bleeding promptly with or without thrombin. In most of the cases the gelatin sponge was liquefied in a few days where it had been in contact with the raw surface of the dermis. In a few instances the gelatin sponge

dried out and formed a firm covering which remained until the donor area was healed.

Gelatin sponge has been used to control bleeding where excessive granulation tissue has been cut away in preparation for skin grafting. Under such circumstances the gelatin sponge is relatively rapidly absorbed within a few days, so that it is not necessary to remove the gelatin sponge preparatory to skin grafting.

Another use for gelatin sponge which we have found is as a vehicle for penicillin. It was used in ten cases and by and large the results were favorable in so far as penicillin can be expected to be of use locally. These cases included infected granulating wounds which were prepared for grafts, and ulcerated lesions of the leg which were refractory to other forms of treatment. The sponge was soaked in sterile physiologic saline solution in which varying concentrations of penicillin were added. After removal of air from the sponge the solution was not expressed from the sponge as was done when it was used for hemostasis. The sponge was then applied on the wound. Some covering dressing was required to hold it in place. Within twenty-four hours the sponge was usually liquefied to a considerable extent wherever it was in contact with the wound. Where the sponge overlapped normal skin it was not appreciably affected. The sponge was usually reapplied daily or at least every other day.

COMMENT

From these experimental studies we have been impressed with the observation that gelatin sponge apparently has hemostatic properties per se. This may be due to the enormous surface area of the myriads of interstices into which the blood may seep. This vast surface area may be a purely mechanical factor which aids in the clot formation from the bleeding wound. We do not wish to underestimate the usefulness of thrombin but merely to point out that what has been considered merely as the vehicle for the thrombin has in itself a hemostatic action which has not been fully appreciated. It is fair to conclude, however, that some additional hemostatic effect is undoubtedly obtained by the use of thrombin which may not have been easily detectable in our work, in view of the extensive data which have been presented in favor of the use of thrombin. It is therefore recommended that thrombin be added to the gelatin sponge wherever it is used in clinical cases for the purpose of controlling bleeding.

According to Frantz the use of thrombin with soluble cellulose is not only unnecessary but also contraindicated. The acid reaction of the cellulose negates the activity of the thrombin and if one uses an alkaline solution as a preliminary rinse before adding the thrombin solution, this nullifies the specific hemostatic action of the cellulose which is a property of the acidity of the material. Furthermore, the best hemostatic action of the soluble cellulose is obtained when it is applied in a dry condition to the bleeding surface.

In the clinical use of gelatin sponge we have been guided by the principle that it should not be relied upon for hemostasis in any condition in which a ligature or suture would ordinarily suffice. It has been used as a supplement to ligature or where ligature was not appropriate. When a large number of

ligatures are concentrated in a relatively small area such as in thyroidectomy, it is desirable to minimize the amount of hemostatic agent which might be required for additional hemostasis, in view of the apparent increase in tendency for serum to accumulate in the wound. It is probable that in thyroidectomy the gelatin sponge should be reserved for such hemostasis as might otherwise present some hazard to the recurrent laryngeal nerves. In view of the experience in which chromic catgut knots were extruded for one month after thyroidectomy where the sponge was used, it is quite probable that this hemostatic agent should be used only very sparingly where a considerable number of cotton or silk ligatures are concentrated. This point will require more attention as any factor which would contribute to the extrusion of silk or cotton ligatures must be carefully evaluated.

In regard to the use of gelatin sponge on skin graft donor areas, it would appear that there are lytic ferments in the dermis to which the gelatin sponge is especially vulnerable. The possibility of utilizing a gelatin sponge which is prepared in such a way that it has a greater resistance to liquefaction under such circumstances is being explored. In its present form, gelatin sponge is not recommended as a dressing for donor areas unless there is some especially troublesome bleeding.

Clinical observations are being made on the use of soluble cellulose which are thus far too limited to include in this report except for the two cases mentioned in which a significant observation was made. It has been necessary to resort to boiling to sterilize the soluble cellulose. It is possible that this may have impaired its hemostatic properties by producing some basic changes in the cellulose. Furthermore, Frantz has found the soluble cellulose to be more effective when used dry. This may account for some of the observations made in this report.

The use of the gelatin sponge as a vehicle for penicillin is of considerable interest as it provides a means of applying the medicament to the wound without subsequently having to remove an adherent dressing which may be painful and which may result in the avulsion of recently formed epithelial cells. It is probable that it would also be suitable as a vehicle for other antibiotic medicaments.

In regard to the relative merits of gelatin sponge and soluble cellulose it is probable that they will be found to have varied uses for which one will be more valuable than the other and vice versa. The wider use of both of these materials by critical surgeons will help to establish the criterion by which one may choose the agent best suited to meet any particular problem of hemostasis.

In neurosurgery the experiences of Pilcher and Meacham and Light and Prentice with gelatin sponge and thrombin have demonstrated this material to be a valuable addition to the armamentarium of the neurosurgeon. This is of particular significance because of the obvious problems involved in the continued production of human fibrin foam which, of course, has been invaluable to the neurosurgeon. It would undoubtedly be of similar value to the general surgeon, in view of the recent report by Bailey, Ingraham, Swenson, and Lowrey, if it were not for the problem of availability.

SUMMARY AND CONCLUSIONS

In a series of thirty animals the hemostatic action of gelatin sponge with and without thrombin was observed. Control studies were made utilizing oxidized or soluble cellulose, and in a few instances fibrin foam.

Gelatin sponge was used in a series of sixty clinical cases for the purposes of hemostasis or as a vehicle for penicillin.

Gelatin sponge appears to have many useful possibilities in the problems of hemostasis in general surgery, where it may prove as valuable as it has been in neurosurgery.

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ADDENDUM

Since this work was submitted for publication some additional data have been obtained. In collaboration with Janda, and subsequently with Senz and Owen, wounds of the vena cava were made in dogs. In twenty-one out of twenty-three experiments the hemorrhage could be controlled by a gelatin sponge "patch" applied over the wound with finger pressure for two to four minutes. This "patch" usually became adherent to the vein, sealing off the wound until it healed over, and subsequently underwent absorption. One secondary hemorrhage occurred in this series. In two instances the hemorrhage could not be controlled.

In collaboration with Senz and Owen, a series of seventeen experimental wounds were made in the aorta of dogs. It was found that the hemorrhage could be controlled and the blood flow restored by a "cuff" of dry, compressed gelatin sponge held in place by four chromic catgut ligatures. Blowouts subsequently occurred after four to six days because of the friability of the sponge. When the sponge was supported by an absorbable sheath of chromic catgut, the blowouts were prevented in nine out of ten animals. In one of these a propagating thrombus was found adherent to the wound in the vessel.

In collaboration with Owen and Senz, wounds of the heart were made in a series of twelve dogs. Some of the wounds were large enough to admit the tip of a finger into the ventricle. The hemorrhage was controlled by the application of a dry, compressed patch of gelatin sponge. After twenty to thirty minutes the patch was usually adherent to the heart. There was no secondary hemorrhage or blowouts in these experiments. The twelve animals of this series survived or were sacrificed from two to forty days after operation.

These additional experiments were done without the use of thrombin and support the view that the gelatin sponge has hemostatic properties per se. This work will be reported in detail elsewhere.

MULTICENTRIC ORIGIN OF INTRAORAL CARCINOMA

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THE present-day treatment of intraoral cancer has resulted in such a discouraging outlook that an evaluation of the factors of therapeutic failure seems indicated. Emphasis has perhaps been placed rightly on the occurrence of cervical node metastases as a cause of failure, but local recurrence is likewise a serious factor in failure of cure. Although in recent years treatment methods used for control of the primary lesion have increased greatly in efficiency, it is obvious that no patient can be cured unless the disease is obliterated at its site of origin. Trite as this may seem, there is a tendency to lose sight of this fact, and to minimize the factor of persistence, or recurrence, of cancer at its primary site. Two recent publications have brought out this factor without emphasizing it. Martin, Munster, and Sugarbaker,[1] in a review of 498 cases of lingual cancer, reported only a 45 per cent rate of five-year cure in 191 patients of this group who never at any time in the course of their disease showed evidence of metastases. Their rate of five-year cure in the 498 patients reported was 25 per cent. In their figures of patients with proved metastases who were not cured, it is not indicated how many had persistent cancer at the primary site. Their reported 45 per cent rate of five-year cure in those patients without metastases would indicate numerically a 55 per cent failure of control of the primary lesion, which indicates a high rate of failure. Lawrence and Brezina,[2] in a review of 108 patients with cancer of the oral cavity treated during a ten-year period at the New Haven Hospital, reported for the entire group a 68 per cent failure to control the primary lesion. This figure includes the earliest treatment, in 1931, and is probably not a fair reflection of more recent results.

These considerations have prompted a study of the causes of failure in control of the primary lesions in patients with intraoral cancer. In the last two years eighty such patients have been treated at the tumor clinics of the Illinois Research and Presbyterian Hospitals. Although not suitable for any kind of end-result reporting, it is already apparent that in this group the experience will be essentially similar to that reported elsewhere.

It must be admitted that poor results are being obtained throughout the country in spite of the fact that during recent years methods of delivery of cancerocidal tumor doses of gamma and x-radiation have been improved, and ingenious operations have been divised to effect anatomic circumvention in the excision of intraoral cancers. This report is concerned with observations of the biologic behavior and histogenesis of these tumors in their relation to local recurrence.

Close observation of the location, patterns of spread, and recurrence behavior of these intraoral cancers has led me to an interpretation of their method

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of growth which is at variance with the generally accepted tenets of cancer teaching. It is generally considered that a malignant tumor grows by multiplication of pre-existing cancer cells, and spreads by invasion and destruction of surrounding tissue. Description of these two mechanisms might constitute a definition of a malignant tumor, but such a simplified concept does not explain all the aspects of the growth and recurrence of carcinomas of the oral mucous membranes. Origin of these lesions from multicentric foci of epithelial change, and their spread by progressive lateral cancerization, is a concept that would explain many of the local recurrences following treatment of intraoral cancer. The term "multicentric origin" refers to the origin of tumor cells at multiple points in a given area of mucous membrane. These separate foci of neoplastic change may be close together in a small area, or widely separated. If close together the separate foci of origin would coalesce as growth proceeded, and form a single tumor. If widely separated, independent multiple tumors would result.

The term "lateral cancerization" refers to growth at the edges of a tumor by a process of progressive transformation into cancer of the epithelium, rather than progressive destruction of the epithelium by pre-existing cancer cells. Lateral cancerization may occur by two methods, either through multicentric foci of independent epithelial change, or through a carcinogenic effect of cancer cells on benign epithelium. This latter mechanism is conjectural, but it is believed that multifocal origin of intraoral cancer is demonstrable. Multiple foci of epithelial change into neoplasia occurs in various stages, and maturation of such a process does not occur simultaneously at various points in a given field of epithelium. Thus, the time element enters and explains the progressive character of such a process. Such a concept of the origin and growth of cancer is contrary, however, to the traditional view of the mechanics of cancer spread.

This concept of lateral cancerization is not new, but has been discussed and dismissed in the older literature as not being correct. Ribbert and Adami have both condemned it. Ewing[3] has entertained it as a possibility for which there is no adequate proof. Recently Brunschwig has reopened the problem and has submitted experimental evidence demonstrating these factors of multicentric origin and lateral cancerization in induced skin cancer in mice, and in a spontaneous skin cancer in a human subject (Brunschwig and Tschetter,[4] and Brunschwig and Thornton[5]). Willis[6, 7] has published a thorough study of the origins and spread of skin cancer in human subjects in which he concluded that such tumors not only arise in multiple foci of origin which coalesce to form a single lesion, but that such lesions increase in lateral extent mainly by progressive transformation into cancer of the marginal benign epithelium.

A study of these eighty cases has yielded data supporting these views as being important factors in the origin and spread of intraoral cancer. This study has been carried out from two standpoints, first, a review of the topography and anatomic extent of the primary lesions and, second, microscopic study of all pathologic material available. In classifying the lesions as to site of origin, the very extensive ones were classified according to the site of the center of the tumor, which seemed appropriate because many of these neoplasms involved widely the mucous membrane of contiguous structures. Two of the patients

TABLE I. TUMORS IN EIGHTY PATIENTS

ANATOMIC DISTRIBUTION		MICROSCOPIC EVIDENCE OF MULTIPLE ORIGIN	GROSS EVIDENCE OF LATERAL SPREAD GREATER THAN DEPTH
Base of tongue	7	0	7
Extensive disease	2	1	2
Soft palate	14	0	14
Central palate	2	1	2
Gingiva	13	8	12
Floor of mouth	5	1	5
Buccal mucosa	5	3	5
Tongue	18	8	11
Multiples	14	9	14
Total	80	31	72

had intraoral cancer of such an extent as to defy classification. These two will be discussed in detail later. The anatomic distribution of the tumors in the cases studied is shown in the first column in Table I. It will be noted that the last entry is listed as multiple tumors. The anatomic location of these multiples is listed separately in Table II.

TABLE II. ANATOMIC LOCATION OF MULTIPLE TUMORS

CASE NUMBER	LOCATION OF TUMORS
1	Tonsil and gingiva
2	Tonsil and gingiva
3	Floor of mouth and tongue
4	Bilateral buccal mucosa
5	Antrum and opposite gingiva
6	Lip and tonsil
7	Floor of mouth and tonsil
8	Tongue and esophagus
9	Lip and buccal mucosa
10	Lip and buccal mucosa
11	Tongue and floor of mouth
12	Bilateral buccal mucosa, tongue, and floor of mouth
13	Tongue anterior and posterolateral
14	Tongue anterior and posterolateral

GROSS APPEARANCE OF TUMORS

Study of the size, shape, and extent of the primary sites of these tumors brings out one finding of significance. The majority of even the advanced and late lesions has a much greater involvement of the surface than of the deep tissues. This characteristic does not seem compatible with the hypothesis that centrifugal expanding growth with invasion and destruction is the only mechanism of local extension of a tumor of mucous membrane. Although tissue barriers, such as bone or fascia, may delay or deflect expansile growth, this does not seem to explain the distinct tendency to lateral spread involving mainly the mucous membrane. Of the eighty cases studied, this tendency to lateral spread in the mucosa was found in seventy-two, as determined by the gross aspect of the tumors in situ. In the third column in Table I is listed the number of tumors, according to primary site, which was considered to show considerably greater lateral extent than extent in depth. This fact alone may or may not be significant as evidence for lateral spread by progressive canceriza-

tion or multicentric origin, but coupled with the microscopic evidence it is at least suggestive.

Two of the patients studied had such extensive cancers that definition of the site of origin could not be made. One was a woman 79 years of age who had had the cancer for over one year; it involved the entire left buccal mucosa, extending

Fig. 1.—Photograph of patient with carcinoma of the tongue. The bulk of the lesion is anterior and it fades out to a flat, granular lesion in its posterior extent.

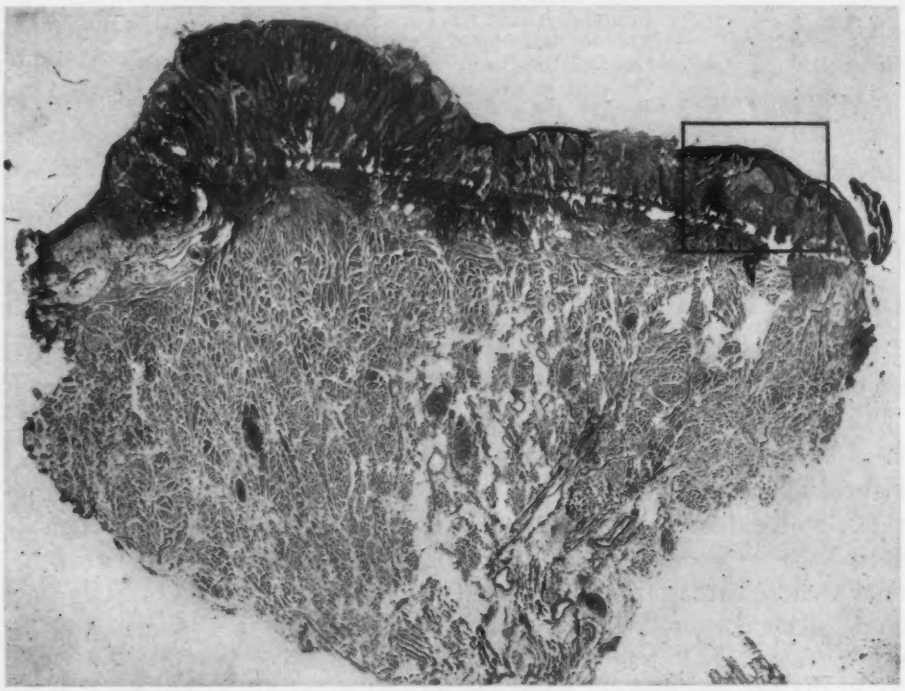

Fig. 2.—Low-power photomicrograph of lesion pictured in Fig. 1. The lesion is seen to be flat, with greater lateral linear extent than extent in depth. The tumor is seen to be involving, and arising from, a broad area of epithelium. In the area boxed there is seen an isolated island of cancer cells arising from the surface epithelium and extending downward in the submucosal tissues. The site of origin of this focus of cancer is surrounded by benign epithelium.

over the vermilion border of the lower lip across the midline, and extending over the upper gingiva on the left to involve the entire left palate, crossing the midline. This lesion was somewhat bulky in the central portion, but for the most part was flat and raised only a few millimeters above the normal mucosal level. Biopsies from multiple areas showed a grade 1 squamous-cell carcinoma. The biopsies, as will be discussed later, showed independent origin of the tumor cells from the surface epithelium in almost all microscopic fields. There was rather extensive leucoplakia throughout the uninvolved oral mucosa. This lesion has metastasized to the cervical nodes since treatment was begun.

Fig. 3.—High-power photomicrograph of area outlined in box in Fig. 2. The area of cancer here is shown to be arising from apparently benign surface epithelium which is in continuity with benign epithelium on either side. Serial sections of this area show the focus of origin to be isolated and not in direct continuity with any other part of the tumor. The scattered areas of cancer aggregates shown here in the submucosa can be shown to be extensions of similar isolated foci of carcinogenesis, arising at scattered, multiple points in the epithelium.

The second patient was a man, aged 56 years, with bilateral cervical node metastases from squamous-cell carcinoma that extended from the floor of the nose bilaterally, to involve the mucosa of the entire nasopharynx and to extend downward on both sides of the posterolateral pharyngeal wall to end in both piriform sinuses. The primary lesion was flat, granular, and clinically resembled rhinoscleroma. Biopsies, however, showed obvious epidermoid carcinoma, and the tumor had metastasized.

These cases have several points in common. First, the tumors were flat, their linear extent and surface area being by far greater than their extent in depth. Second, the peripheral limits of each tumor were in locations which could not possibly have been reached by expansion and invasion from a central

source. Neither were they in areas to which metastasis could occur. A process of progressive lateral cancerization seems to be the only reasonable explanation that could account for such distribution.

MULTIPLE TUMORS

Previous studies[8] of multiple tumors have proved that this phase of the multicentric origin of tumors is more important than has been generally appreciated. In the patients reviewed in this study, fourteen out of eighty had

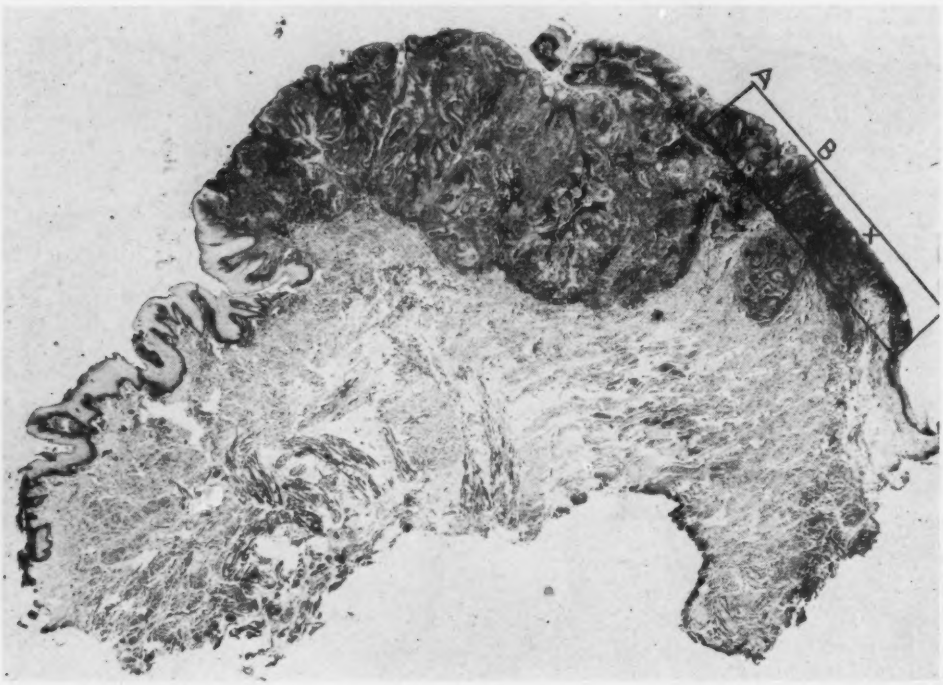

Fig. 4.—Low-power photomicrograph of cross section of excised carcinoma of the tongue. The lesion is shown to be moderately infiltrating, but still of distinctly greater lateral extent than extent in depth. At either margin of the carcinoma there is a wide area of benign but thickened and hyperplastic epithelium. The boxed area to the right includes an extension of the lesion which is noninfiltrating and represents intraepithelial epidermoid carcinoma in situ.

multiple, independent malignant tumors involving the oral or pharyngeal mucosa, an incidence of approximately 18 per cent (Table II). These patients had multiple epidermoid carcinomas so situated that one lesion could not have originated by direct extension from the other. There are two possibilities which could relate such lesions, either lymphatic metastasis to other areas of mucosa, or implantation of surface cells carried by the oral secretions. The well-known metastatic patterns of intraoral cancer make it highly unlikely that metastasis would or could appear in separated areas of mucosa, particularly in the opposite side of the mouth. As to the implantation of cancer cells into a normal, or even broken mucosa, experimental evidence and experience with transplantation of animal tumors make this so improbable that it practically can be precluded even as a possibility. None of the multiple tumors described herein were of the so-called "kissing cancer" type, that is, representing two tumors lying in contact

with each other but with no neoplastic connections. Whether or not this is implantation cancer is debatable, therefore, these fourteen patients are described as having true multiple tumors. Such cases demonstrate the factor of multicentric origin, and their incidence of 18 per cent in this small series indicates the importance of such a factor in tumor growth, although the number of cases is too small to be of serious statistical significance.

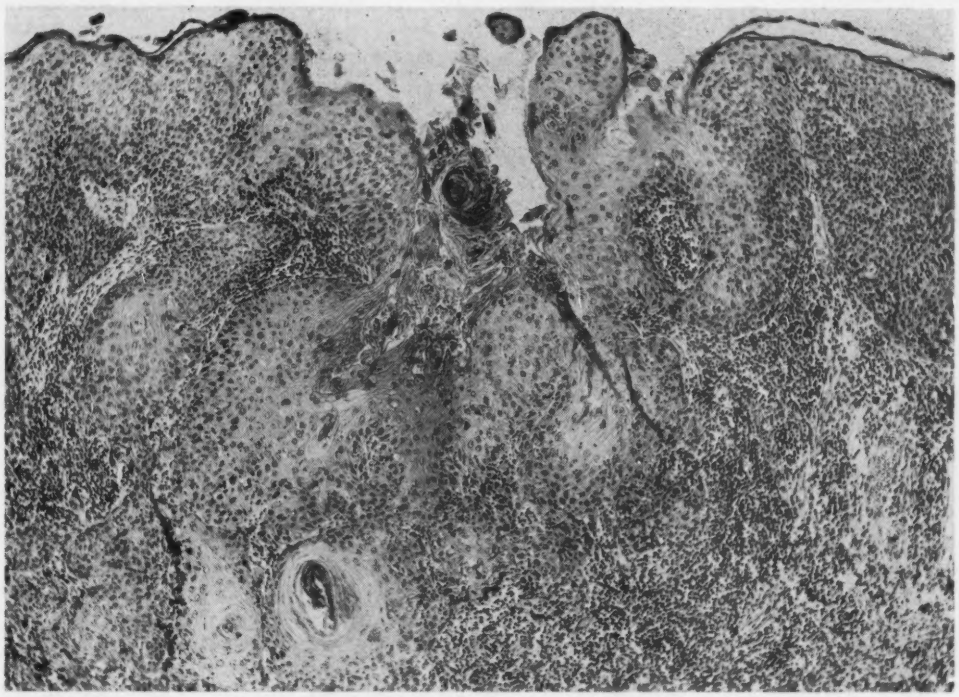

Fig. 5.—High-power photomicrograph of area boxed in Fig. 4, extending from *A* to *B*, This is the junctional zone between the infiltrating and keratinizing epidermoid carcinoma to the left and the intraepithelial cancer to the right, whose extent is delimited by the area of the box in which point *x* is located.

The majority of these patients with multiple tumors had only two separate lesions. One patient, however, had seven intraoral cancers in three years. When first seen, at the age of 30, she had an extensive squamous-cell carcinoma involving most of the right buccal mucosa, which was treated with intraoral x-radiation. There was fairly extensive leucoplakia throughout the oral mucosa. She remained well one year and then complained of severe pain in the opposite cheek. This pain continued and a trophic ulcer appeared in the left buccal mucosa, opposite the area previously treated. Biopsy of this revealed no cancer, but three months later the lesion was excised and at that time was composed of undifferentiated epidermoid carcinoma. One year later the patient presented five new and separate small foci of carcinoma. One was located on the dorsum of the tongue and measured 2 cm.; one was on the right tonsil, measuring 5 mm.; one was in the right floor of the mouth, measuring 1 by 1.5 cm.; and two minute areas were on the buccal side of the mucosal lining of the lower lip, in the anterior gutter. These were biopsied and treated with radon seeds with com-

plete regression. At the time of death this patient was clinically free of intraoral cancer, but she had advanced bilateral cervical node metastases. Biopsies of two of these lesions showed what appeared to be origin of the carcinoma in several foci from the overlying surface epithelium. The leucoplakia in this patient's mouth was extensive, and after observing her throughout the disease, one had the feeling that almost the entire oral mucosa in this patient would eventually have undergone malignant transformation had she lived long enough.

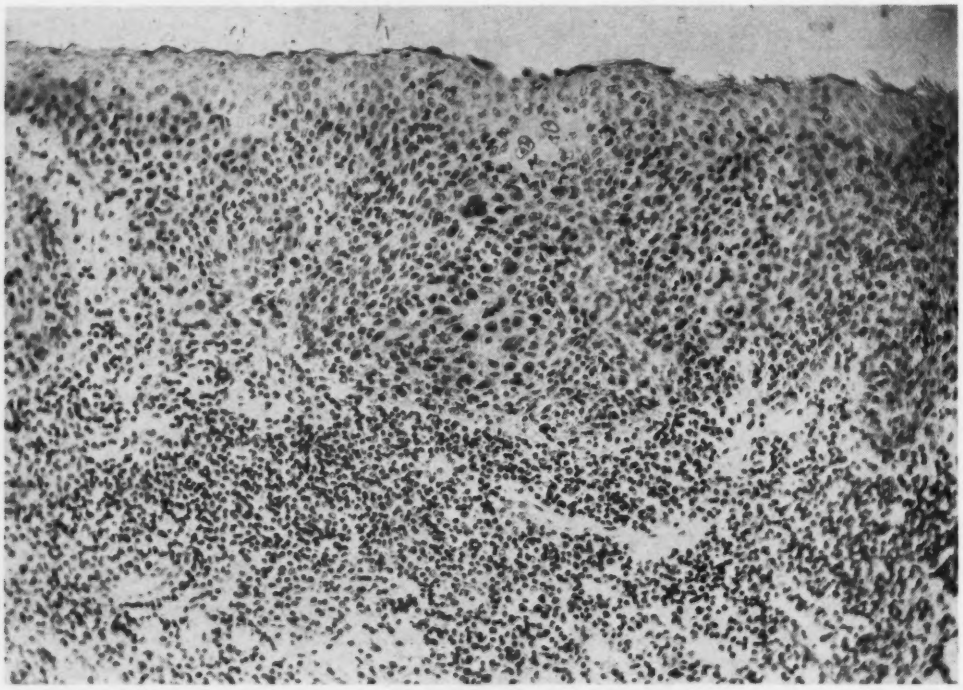

Fig. 6.—High-power photomicrograph of epithelium at point marked *x* in Fig. 4. Here is shown intraepithelial epidermoid carcinoma in situ. As seen in Fig. 4, this area extends for some distance past the invading cancer.

MICROSCOPIC FINDINGS

Study of the pathologic material available on the eighty patients in this series produced further evidence indicating that multicentric origin and/or lateral cancerization are factors operating in the spread and growth of intraoral cancer. Since the treatment of intraoral cancer is mainly by irradiation methods, only small biopsy specimens were available for study from most of the tumors. These biopsies were routine specimens and were not removed in any deliberate manner with this study in mind. In fourteen of the patients complete excision was done, and in these cases the entire excised tumor was available for study. The microscopic examination was carried out with three points in view; first, evidence of origin of tumor from superficial epithelium, especially in more than one area; second, study of the junctional zone between benign and malignant epithelium; and third, the condition of the epithelium in the benign periphery of the tumor.

Biopsy Specimens.—The small biopsy specimens were not very satisfactory for study because most of them were taken from the central ulcerated area of the tumor and showed nothing but solid tumor tissue, from which no conclusion could be drawn other than the diagnosis of cancer. Twenty-one of the small biopsies, however, which included nonulcerated tumor or some benign epithelium showed evidence of origin of the malignant cells from the overlying surface epithelium in two or more areas. Such evidence was based on the presence of

Fig. 7.—Cross section of excised mandible with recurrent carcinoma of the overlying gingiva and adjacent buccal mucosa (see text for history of case illustrated in this and the following figures). The alveolar ridge is gone, from previous tumor and radiation, and the "recurrent" tumor is seen to be confined to the epithelium and submucosa. To the right the epithelial change can be seen extending upward onto the buccal mucosa. The epithelial change is a diffuse one and in this section appears to be arising at many separate points.

microscopic fields with tumor cells showing invasion beyond the basement membrane of apparently benign surface epithelium, the invasive cells being in direct continuity with the overlying epithelium. Most of the sections showed areas which, taken alone, would represent "early cancer." The surface epithelium is eventually destroyed by extensive growth, but in early lesions the tendency is downward and not upward invasion. It is, therefore, considered reasonable to believe that small cell nests exhibiting downward invasion through

the basement membrane, but still in continuity with the epithelial layers, are evidence of origin of these cells from the epithelium at that point. Demonstrable isolated origin of tumor cells from the surface epithelium in only one section is inferential evidence of multicentric origin of the tumor, because the rest of the tumor must have come from other cells. The presence of two or more areas showing origin of tumor cells from the surface epithelium is more adequate evidence of multicentric origin. It is probable that biopsies taken deliberately from the periphery of tumors, and in larger sections, would show microscopic evidence of multicentric origin in a considerably higher proportion of the tumors. Study of the totally excised lesions would tend to bear this out.

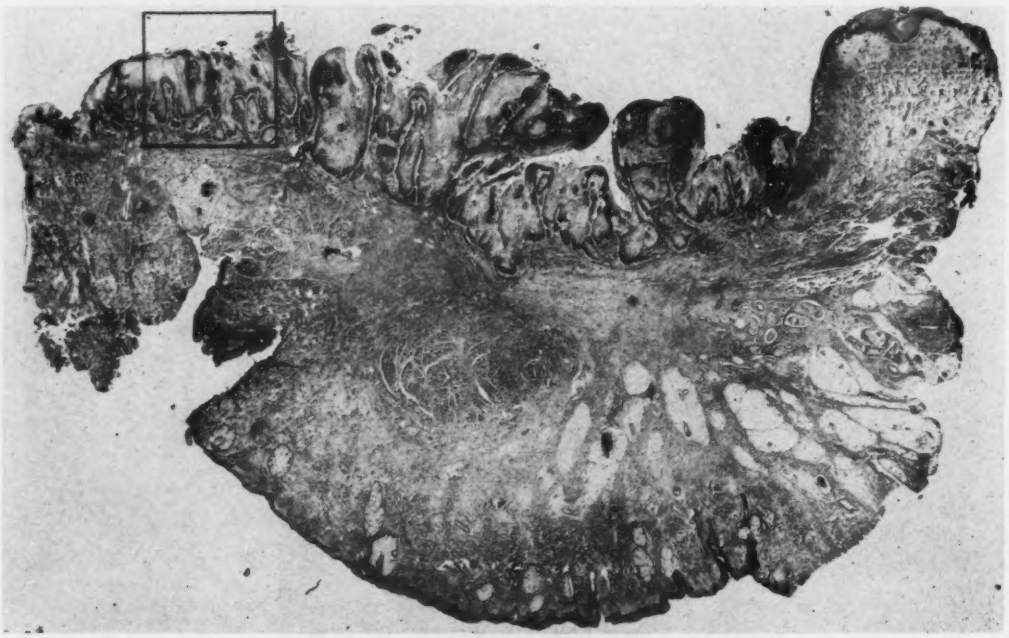

Fig. 8.—Low-power photomicrograph of full thickness of cheek excised in continuity with the mandible shown in section in Fig. 7. The top surface shows replacement of the epithelial layer by a diffuse, low-grade epidermoid carcinoma. This area of the tumor is in part intra-epithelial in situ cancer and partly invasive. Such an area of tumor could hardly have arisen from one cell or from one small area. The picture of atypism to a degree diagnosable as carcinoma is essentially in the basal cell layers, while the superficial layers are apparently still benign and nonulcerated.

Surgical Specimens.—Fourteen specimens excised from the eighty patients were available for study. Thirteen of these specimens showed microscopic evidence of origin of the tumor at multiple points from the superficial epithelium. Thirteen of them showed lateral linear extent considerably greater than their extent in depth. The thirteen neoplasms in each list are not identical, as one tumor of the flat type did not show origin of tumor cells from the surface epithelium, and the one tumor of the invasive and expansile type did show such a picture. Obviously there was some difference in the clinical picture of the fourteen patients treated surgically as compared to the sixty-six patients treated by irradiation. In six of the patients the tumors were treated by surgical methods because the lesions had failed to respond to irradiation or had "re-

curred'' following irradiation, and in all six, bone was invaded by cancer. The other eight cases consisted of five small or superficial and accessible epidermoid carcinomas of the tongue, one of the buccal mucosa of the upper lip, and two of the buccal mucosa with invasion of the maxilla when first examined. Decision to utilize surgical excision primarily for the five lingual cancers was prompted by their accessibility, ease of removal, and quick healing as compared with the prolonged discomfort following radiation of such lesions.

Examination of the cross sections of these excised carcinomas showed that all except one were relatively flat, superficial tumors whose lateral linear extent was greater than their extent in depth. Higher power fields showed them to be unmistakably malignant and invasive, but it was equally obvious that the change was a diffuse one over a wide extent of epithelium. At the margins of the malignant tumor, the transition into benign epithelium was abrupt, yet for a variable distance this benign epithelium showed distinct hyperplasia. In a few

Fig. 9.—High-power photomicrograph of area boxed in Fig. 8. Here is shown both invasive and preinvasive epidermoid carcinoma. The epithelial change is a diffuse one involving many cells at once, and the neoplastic activity is not arising from any central source of centrifugal expansion.

sections this hyperplasia was atypical, and in some could be classified as intraepithelial carcinoma in situ. In three of the lesions excised primarily, there were areas of benign epithelium interspersed between areas of frankly invading cancer (Figs. 1 to 6). In the one tumor which on cross section showed invasion equal to lateral extent, the junctional zone between malignant and benign epithelium showed what was interpreted as evidence of origin of the tumor cells from the surface epithelium.

The most thought-provoking finding from this study is the evidence of multiple origin of tumor cells from the surface epithelium in the recurrent cancers. Of the six lesions excised because of "recurrence" and bone invasion, three actually represented persistence and/or growth and extension during and after irradiation. The other three tumors recurred one, one and one-half, and three years, respectively, following the original therapy. The usual concept of local recurrence of cancer is that it is due to residual cells not removed by surgery, and not destroyed by irradiation; these cells resume their growth capacity and produce a new tumor as a continuation of the original one. The findings here recorded by no means invalidate this concept, but they do suggest that there may be another mechanism which occasionally explains the recurrence of intraoral epidermoid carcinomas. This mechanism would be the progressive transformation into cancer of benign epithelium which has healed over the site of a destroyed cancer.

One case particularly illustrated the possibility of such a mechanism. The patient had an epidermoid carcinoma of the right lower gingiva, with erosion and exposure of the underlying alveolar ridge. In spite of the evidence of bone involvement, he was treated with x-rays through an intraoral cylinder with apparently complete regression of the tumor. Within six months after the radiation reaction had subsided the *area was healed* and the exposed bone covered by epithelium. Three months later the area irradiated was covered with fairly heavy leucoplakia. This was biopsied at a subsequent visit and proved to be benign hyperplasia. Three months later the leucoplakia had become much thicker and had extended across the buccal gutter well up on the buccal mucosa. Biopsy now showed squamous-cell carcinoma. Excision of full thickness of the cheek and the mandible was carried out. Sections of the tumor are shown in Figs. 7, 8, and 9. The low-power view of the whole thickness of the cheek showed a low-grade, superficial, extensive epidermoid carcinoma, intraepithelial in some areas and invasive in others. The topography of the lesion made it improbable that such a neoplasm could have arisen either from one or many tumor cells which retained their growth potential following the original roentgen treatment. It is equally unlikely that such a tumor could have originated from a single central source, either of residual cancer or of an entirely new tumor.

DISCUSSION AND IMPLICATIONS

Study of the anatomic extent and gross appearance of the tumors in eighty patients with intraoral cancer showed that the majority of such lesions were relatively flat with definitely greater linear extent than extent in depth. In 18 per cent of the eighty patients there occurred at least two epidermoid carcinomas, separated by areas of normal mucosa adequately wide to allow definition of them as independent lesions. In the small biopsies from this series of patients, there was found evidence in twenty-one of origin of tumor cells from the benign surface epithelium in more than one area. Fourteen of the patients had surgical excision of the tumors. In this group thirteen showed lateral extent greater than depth, and thirteen showed origin of the tumor from multifocal contiguous areas of surface epithelium. Some of these foci of origin in the

periphery of the tumors were isolated and surrounded by benign epithelium. In every instance where the entire tumor was available for study, the peripheral benign epithelium was found to show a marked degree of hyperplasia, atypical in a few instances to a degree allowing the diagnosis of intraepithelial carcinoma in situ.

These three factors, namely, lateral spread, multiple tumors, and microscopic evidence of multicentric foci of origin, would seem to suggest that another mechanism occasionally exists regarding the growth and spread of intraoral epidermoid carcinoma.

That the tumors illustrated here could arise from one cell, or one small focus of carcinogenesis, seems unreasonable. There is no question that a malignant cell divides and reproduces in a biologically relative form of geometric progression, yet this mechanism alone does not explain the behavior nor the distribution pattern of the epithelial changes in intraoral cancer.

These considerations also tend to show that epidermoid carcinoma not only does not arise from a single small focus in space, but neither does it arise in a single small unit of time. The sections represented here demonstrate multiple phases of epithelial change through all stages of carcinogenesis, from early reversible hyperplasia to frankly invading squamous-cell carcinoma. The process is a progressive one, both in a given field of tissue and in time relationship.

Horizontal spread of intraoral cancer by a process of progressive lateral cancerization would seem to be a double process, consisting of the division, growth, and multiplication of existing cancer cells, plus formation of a new foci of malignant neoplastic activity in the periphery of a tumor. This latter process is probably a self-limited one in time and space and is mainly demonstrable only in fairly early tumors. However, where a wide field of mucosa has been conditioned to progressive epithelial neoplasia, local "recurrences" of a tumor after treatment may often represent new foci of cancer arising independently at the edge of the treated or excised area.

There is suggestive evidence that recurrence of a carcinoma within the site of a previously treated tumor may be due to late neoplastic change occurring in epithelium which has grown in from the edges and covered the site of a previously destroyed tumor. Such epithelium may respond to the wound healing stimulus, retaining its latent neoplastic potential which later becomes manifest as "recurrence." Recurrent tumors frequently appear as superficial ulcerations, and not uncommonly are preceded by visible epithelial change in the form of leucoplakia. This possibility needs further observation and investigation.

SUMMARY AND CONCLUSIONS

Eighty patients with intraoral epidermoid carcinoma have been studied from the standpoint of origin and method of growth of their tumors, and in relation to local recurrence following treatment. The study resulted in three findings: first, most of the tumors were flat, with greater surface extent than

depth; second, 18 per cent of the patients had multiple independent primary tumors; third, microscopic study of biopsies and of whole specimens removed surgically shows evidence of multicentric origin of these epidermoid carcinomas. This multifocal origin is in relation to both space and time. The three sets of data together are evidence that many so-called local "recurrences" may in reality be new foci of cancer arising in the peripheral field of a previously treated tumor.

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PENICILLIN-PHTHALYLSULFATHIAZOLE ANTAGONISM

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THE bacterial flora of the gastrointestinal tract is altered by the oral administration of sulfasuxidine and sulfathalidine[1, 2] by lowering the gram-negative organisms and anaerobic bacteria. The sulfonamides have little or no effect on gram-positive organisms, especially *Streptococcus faecalis* and members of the Salmonella group of organisms.

Penicillin has activity against some organisms not affected by the sulfonamides. It has been demonstrated that penicillin is presumably destroyed by an enzyme, penicillinase, formed by *Escherichia coli*. After the number of

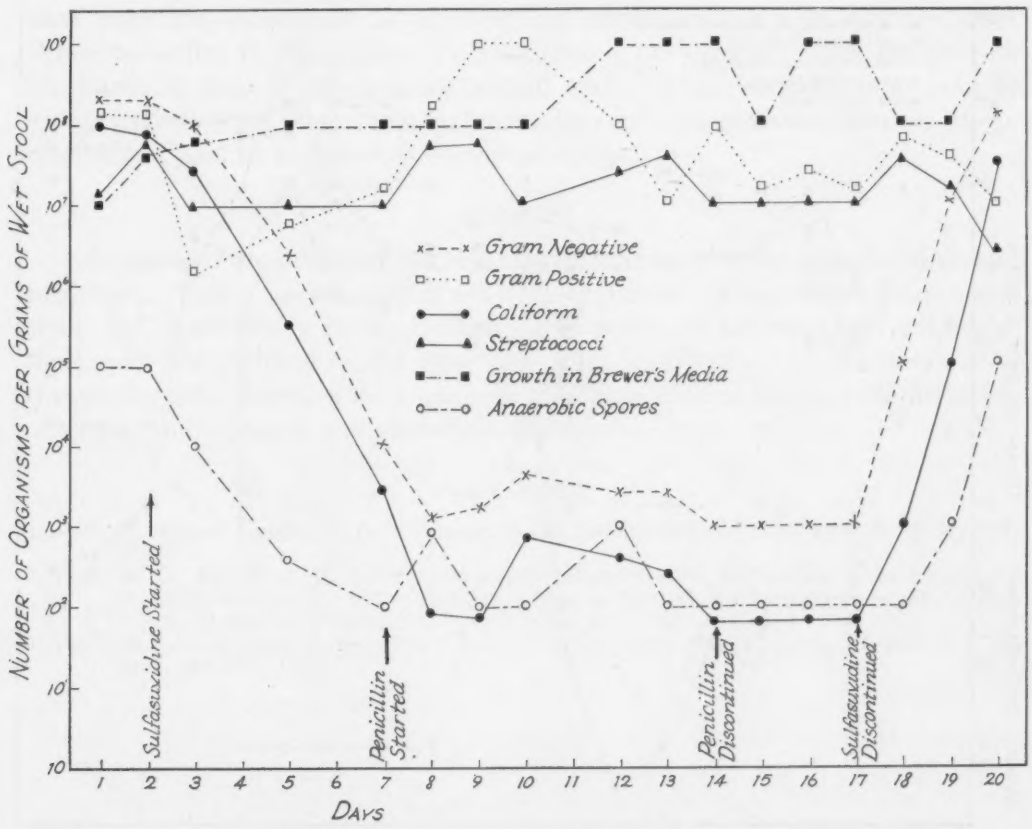

Fig. 1.—Chart illustrating the characteristic alteration of the bacterial flora of the bowel when 3.0 Gm. of sulfasuxidine (succinylsulfathiazole) are given orally to an adult man every four hours, and the fact that the simultaneous intramuscular administration of 20,000 units of penicillin every two hours induces no further change in either the gram-negative or gram-positive flora.

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gram-negative and coliform organisms in the bowel have been reduced by the sulfonamides, it was hoped that penicillin may then be effective against the remaining gram-positive flora. With this concept in mind, sulfasuxidine and sulfathalidine were administered orally to reduce the coliform organisms and then penicillin, 20,000 units, was given intramuscularly at two-hour intervals while the administration of the sulfonamide was continued.

This therapy failed to alter the gram-positive flora of the gastrointestinal tract. There was no demonstrable effect on the reduced flora induced by the administration of sulfasuxidine (Fig. 1). But, when penicillin was given after the bacterial flora had been altered by the oral administration of sulfathalidine, there was a very considerable and unexpected change. The gram-positive organisms were not affected, but there was an abrupt and significant increase in the coliform flora (Fig. 2). There was no increase in the number of anaerobic spores, which had been reduced by the action of the sulfathalidine. Occasionally the number of anaerobic spores was further reduced by the penicillin. The in-

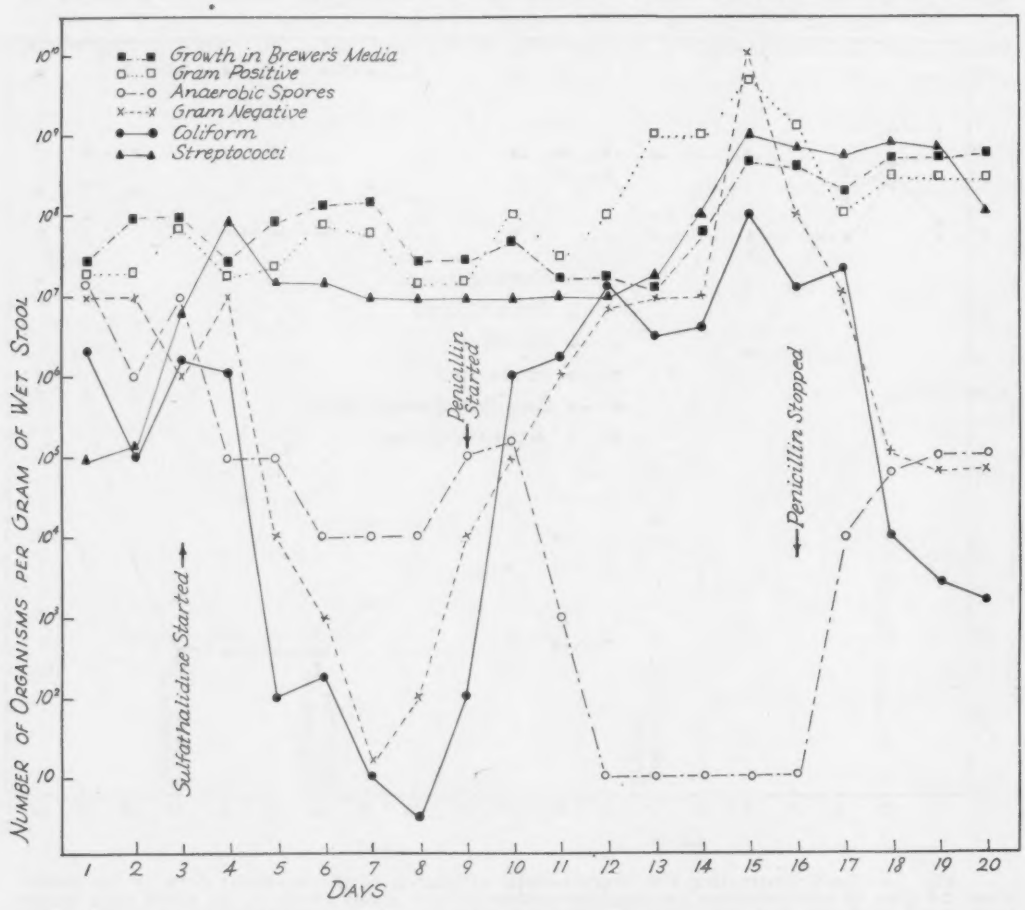

Fig. 2.—Chart illustrating the characteristic alteration of the bacterial flora of the bowel of the adult man when 1.5 Gm. of sulfathalidine (phthalylsulfathiazole) are given orally every four hours, and the fact that the simultaneous intramuscular administration of 20,000 units of penicillin every two hours induces no changes in the vegetative gram-positive flora but does cause a rather striking and unexpected increase in the gram-negative flora to neutralize the bacteriostatic effect of sulfathalidine.

crease in the coliform flora is usually represented by *Aerobacter aerogenes*, although there may be an increase in *Esch. coli*.

These phenomena have been observed on eleven consecutive patients, six of whom received sulfathalidine and five sulfasuxidine. The coliform organisms were isolated and tested for increased resistance to the bacteriostatic action of penicillin and sulfathiazole. In vitro studies failed to show any antagonism between these two substances.

DISCUSSION

The antagonistic action between sulfathalidine and penicillin has not been explained. The antagonism does not exist in the case of the spore-forming anaerobes.

These observations again demonstrate that the entire bacteriostatic action of sulfasuxidine and sulfathalidine is not dependent upon the hydrolysis of these two compounds to yield sulfathiazole.[3]

If it is important to maintain a reduction of the coliform flora of the bowel, then penicillin should not be administered simultaneously with sulfathalidine. When penicillin is being given, sulfasuxidine is the drug of choice for altering the bacterial flora of the gastrointestinal tract. These considerations may be especially important when these sulfonamides are being given in chronic coliform cystitis and pyelitis and chronic ulcerative colitis.

SUMMARY

An antagonism of action has been found to exist between sulfathalidine and penicillin. This phenomenon has not been explained. These observations again stress the dissimilarity in the mechanism of action of sulfasuxidine and sulfathalidine. Penicillin does not alter the gram-positive flora of the bowel even though the gram-negative flora has been strikingly altered by the administration of succinylsulfathiazole and phthalylsulfathiazole.

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DIFFERENTIAL SPINAL BLOCK

A Preliminary Report

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THE introduction of anesthetic agents into the spinal canal has, up to the present time, constituted an important aid to the surgeon in providing a useful type of anesthesia. However, from the physiologic point of view, this simple procedure is perhaps an unrefined technique. Possible differences in susceptibility of the various kinds of fibers that traverse the subarachnoid space have not yet been adequately studied. If such differences in susceptibility should be established, the technique of subarachnoid injection would become more important as a therapeutic and diagnostic tool than it now is.

Anatomic consideration of the nerve fibers in the subarachnoid space, indicates that it should be possible to introduce into the spinal canal a concentration of procaine which would block autonomic nerves while affecting other types of fibers minimally or not at all.[1] This report is concerned with attempts to demonstrate this.

Gasser and Erlanger,[2] working with cocaine, and Heinbecker, Bishop, and O'Leary,[3] working with procaine, have demonstrated that the class C fibers, the least myelinated of a mixed nerve are the first to be blocked when subjected to local infiltration with the anesthetic agent. It does not necessarily follow that these fibers (in which class autonomic fibers generally fall) are blocked by a lower concentration, but it does suggest that this is so and that, therefore, these fibers could be preferentially blocked.

Preliminary experiments in the cat indicated that this was true, since a powerful sympathogenic reflex, the carotid sinus reflex, could be abolished in the vagotomized cat by a 0.15 per cent procaine perfusion of the spinal canal (after the method of Co Tui[4]), at a time when the animal maintained spontaneous respiratory activity and gave a contralateral muscular response to the electrical stimulation of one femoral nerve.

MATERIAL AND METHOD

Six patients from the surgical wards of the Massachusetts General Hospital served as subjects. All were men ranging in age from 30 to 81 years, the average being 53 years.

At the beginning of the observational period the patient was brought into a room in which the temperature was constantly maintained at a given low level (between 15 and 20° C.). The patient wore only a loin cloth. A needle was introduced into the spinal canal between the third and fourth lumbar vertebrae and connected with rubber tubing for continuous intraspinal administration

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after the method of Lemmon.[5] Administration of procaine solution of the desired concentration and at any desired rate was then accomplished using the method and equipment described in a previous communication.[6-8]

Eight thermocouples were then placed as follows: one thermocouple on the plantar aspect of each great toe, one on the lateral aspect of the dorsum of each foot, one each on the palmar aspect of the right thumb and middle finger, and two in different parts of the room. The thermocouples were connected to a device which continuously recorded their temperatures and they remained in place for the duration of the experiment. The recording device was then started and adequate control levels were obtained. At this time the initial dose, 10 c.c. of a 0.2 per cent solution (20 mg.) of procaine hydrochloride, was run in in about three minutes. Thereafter 15 drops per minute (0.6 c.c. or 1.2 mg.) were allowed to run in until the desired effect or height of block was attained. The subsequent rate of administration was determined by the duration and level of the block desired. Blood pressure, pulse, and neurologic observations were made at regular intervals. In one patient determinations of the cerebrospinal fluid pressure were carried out by temporarily connecting a spinal manometer to the segment of tubing connected with the spinal needle.[22] The zero point for the manometer was arbitrarily chosen as the level of the skin of the back so that all observations were a few centimeters too high, although relative deviations were accurately reflected. No other medication was given at any time.

The neurologic examination used during the course of these experiments was as follows: The appreciation of pinprick was elicited with a sharp needle; touch was ascertained by using the blunt end of the needle, a delicate camel's-hair brush, and finger pressure. Proprioception was determined by examining the patient's appreciation of toe position. Vibratory sense was examined by the use of the 256 tuning fork. Heat and cold sensation were examined by the use of heated and cooled steel rods. It should be mentioned that, at the temperature at which these experiments were conducted, the proper appreciation of heat and cold was impaired prior to the induction of the differential spinal block. Therefore, in subsequent parts of this paper when it is stated that there is loss only of pinprick sensation, it should be remembered that impairment of temperature sense also may have been present. In each of the six cases studied the patient volunteered the information that his feet were getting warm when the skin temperature rose and were getting cold again when the skin temperature began to fall (in those cases in which it declined appreciably toward the end of the experiment). At regular intervals the patient was asked to flex and extend his foot maximally and to roll his thighs medially and laterally as far as they could be rolled. He was asked to tense his abdominal muscles and to perform a full inspiration. The deviations from this outline in method are specified in the case reports.

The work of Landis and Gibbon[9, 10] and of Morton and Scott[11] indicates that in an individual in whom the skin temperature has been brought to below 24° C., any factor which then causes the skin temperature to rise to 31.5° C. or above may be assumed to have caused a complete block of the vasoconstrictor nerve fibers to that area. We attempted to meet these criteria in our experiments.

RESULTS

The results indicate that a block of sympathetic fibers and those carrying impulses concerned with the appreciation of pinprick can be accomplished without affecting other forms of sensation (with the possible exception of thermal sense) or motor power, in so far as these impulses are reflected by the neurologic examination used.

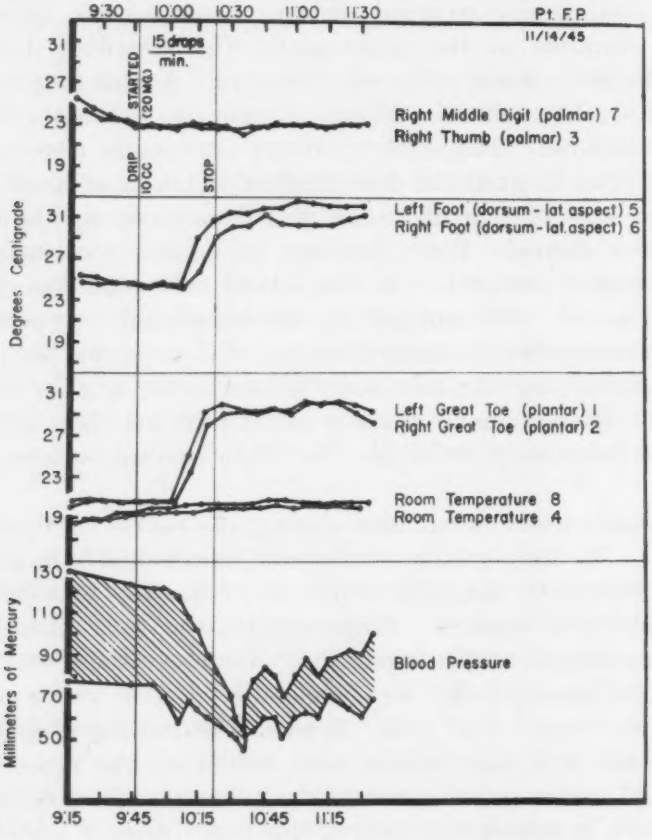

Fig. 1.

CASE REPORTS

CASE 1 (No. 506033).—F. P., 62 years of age, had carcinoma of the stomach (preoperative) (Fig. 1). A lumbar puncture was performed at 9:10 A.M. and, satisfactory skin temperature levels being obtained, the initial dose of procaine was administered at 9:47 A.M. This was 250 drops (10 c.c. or 20 mg.) and took three minutes to run in. The drip was then continued at the rate of 15 drops (0.6 c.c. or 1.2 mg.) per minute. At 10:03 A.M. the skin temperature of the toes rose sharply. The skin temperature on the dorsum of the feet rose shortly thereafter. The temperature of the right hand remained the same. Coincident with the sympathetic block there was a barely discernible diminution of sensation of pinprick on the medial side of the upper portion of each thigh. There was no other loss of sensation and no apparent loss of motor power. Paralleling the rise in skin temperature there was a sharp fall in blood pressure. The sympathetic block persisted for 1.5 hours. Nausea and vomiting were not present at any time. The patient received a 20 mg. initial dose and a 60 mg. total dose over a period of thirty-five minutes.

CASE 2 (No. 436614).—G. H., 30 years of age, had a hemorrhoidectomy (seven days postoperative) (Fig. 2). A lumbar puncture was performed and a continuous spinal needle was inserted between the third and fourth lumbar vertebrae at 10:40 A.M. At 11:11 A.M., 10 c.c. (20 mg.) of procaine hydrochloride were allowed to run in. The drip was then set at 15 drops per minute. At 11:50 A.M. the rate was changed to 20 drops per minute and at 11:53 A.M. there was a sharp rise in skin temperature of both lower extremities. Twenty-three minutes prior to the rise in skin temperature, impairment of the appreciation of pinprick began to manifest itself in the first sacral segment. This increased and at the time of the rise in skin temperature it was at the level of the eleventh thoracic vertebra. The temperature of the right hand remained the same throughout the experiment. There was no other loss of sensation and there was no loss of motor power at any time during this experiment. Paralleling the rise in skin temperature there was a moderate fall in blood pressure which rose again as the skin temperature fell. The patient received a 20 mg. initial dose and a 131 mg. total dose over a period eighty-two minutes.

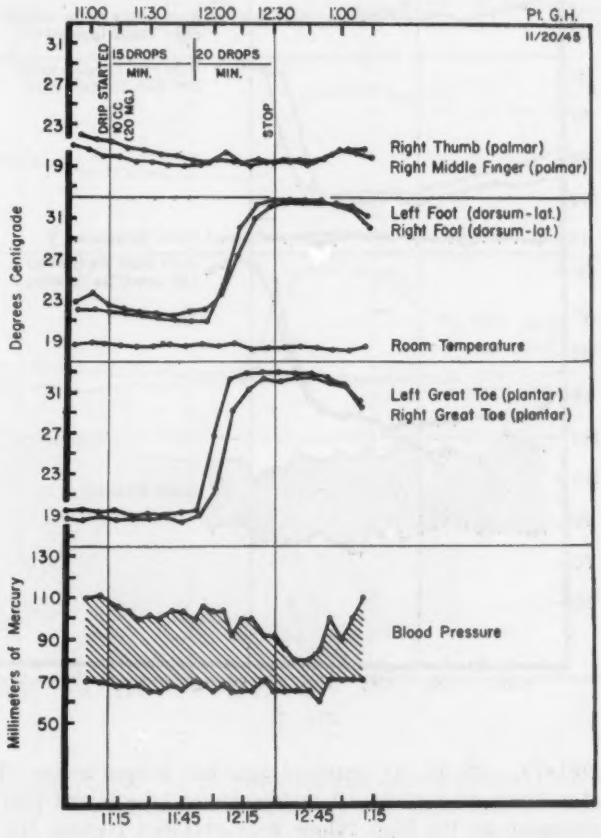

Fig. 2.

CASE 3 (No. 511980).—W. M., 38 years of age, had a right inguinal hernia (preoperative) (Fig. 3). Satisfactory skin levels having been obtained, the intraspinal drip was begun at 11:27 A.M. Between then and 11:30 A.M. 300 drops (12 c.c. or 24 mg.) were allowed to run in. The dripper was then regulated at 20 drops per minute. At 12:11 P.M. the skin temperature of both feet rose sharply. The drip was discontinued at 12:45 P.M. Twenty-six minutes prior to the rise in skin temperature there was beginning, spotty impairment of appreciation to pinprick in the right lower leg. This gradually rose and at 12:55 P.M. it was at the fourth thoracic segment. The temperature of the right hand remained the same throughout. There was no other loss of sensation and no loss of motor power at any time during the course of

this experiment. There was a slight fall in blood pressure paralleling the rise of the skin temperature to the lower extremities and this was accompanied by slight nausea and vomiting. The initial dose was 24 mg. of procaine hydrochloride. The total dose was 144 mg. of procaine hydrochloride over a period of seventy-eight minutes. The patient received a larger initial dose in terms of cubic centimeters as well as procaine hydrochloride and a larger total dose than any other patient in this series. Measurements of the cerebrospinal fluid pressure showed that immediately after the initial dose there was a 6.5 cm. rise in pressure and at the end of the infusion there was a 1.5 cm. rise as compared to the pressure before any infusions were given.

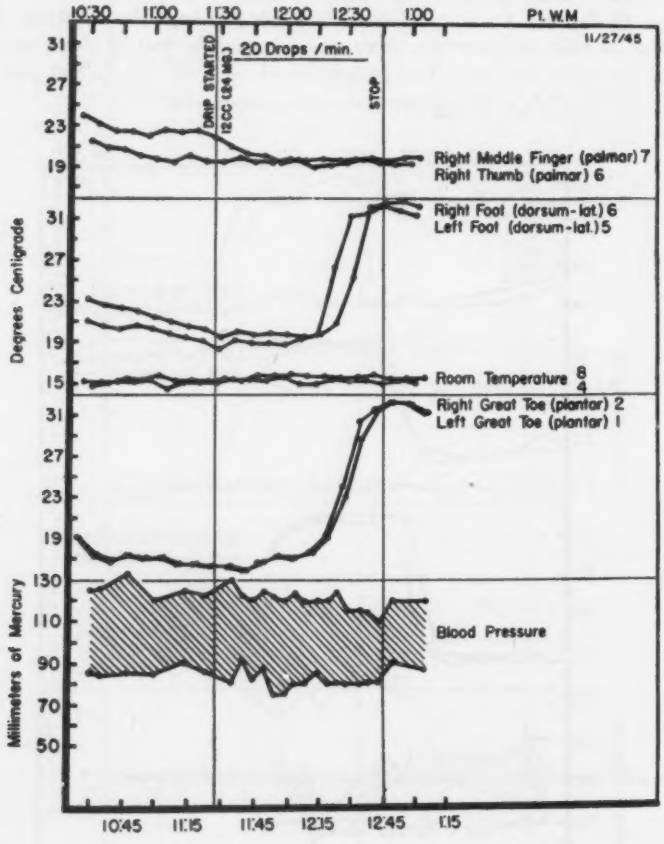

Fig. 3.

CASE 4 (No. 381479).—S. B., 81 years of age, had herpes zoster (Fig. 4). The skin temperature values for the right thumb and middle finger (the initial portion of Fig. 4) are to be disregarded inasmuch as the high values were obtained because the hand was allowed to lie on the chest. When it was removed from the chest the skin temperature fell promptly to 23° C., as is seen in Fig. 4. The initial dose of 8 c.c. of a 0.2 per cent solution failed to produce a rise in skin temperature although gradually diminishing appreciation of pinprick became apparent thirty minutes after the initial dose was given. The initial dose was followed by the administration of 6 drops per minute and at 10:54 A.M. was changed to 10 drops per minute. At 11:30 A.M. this was raised to 12 drops per minute and at 11:53 A.M. to 15 drops per minute. This failed to induce a rise in skin temperature, and a 0.3 per cent solution was run in. The rate was then continued at 10 drops per minute. At 12:45 P.M. the skin temperature of the feet rose sharply and there was a diminution of pinprick up to the level of the sixth thoracic vertebra. There was no other loss of sensation. There was no loss of motor power at any time during the course of this experiment. The dripper was stopped at 1:44 P.M.

Paralleling the rise in skin temperature there was a sharp fall in blood pressure which rose again when the skin temperature began to come down. There were slight nausea and vomiting at the height of the sympathetic block.

This experiment was the first performed and accounts for the cautious initial dose and drop rate administered in the first portion of the experiment.

The preceding four experiments demonstrate that the lower portion of the thoracolumbar outflow was paralyzed in so far as this is indicated by a paralysis of the peripheral vasoconstrictor fibers.

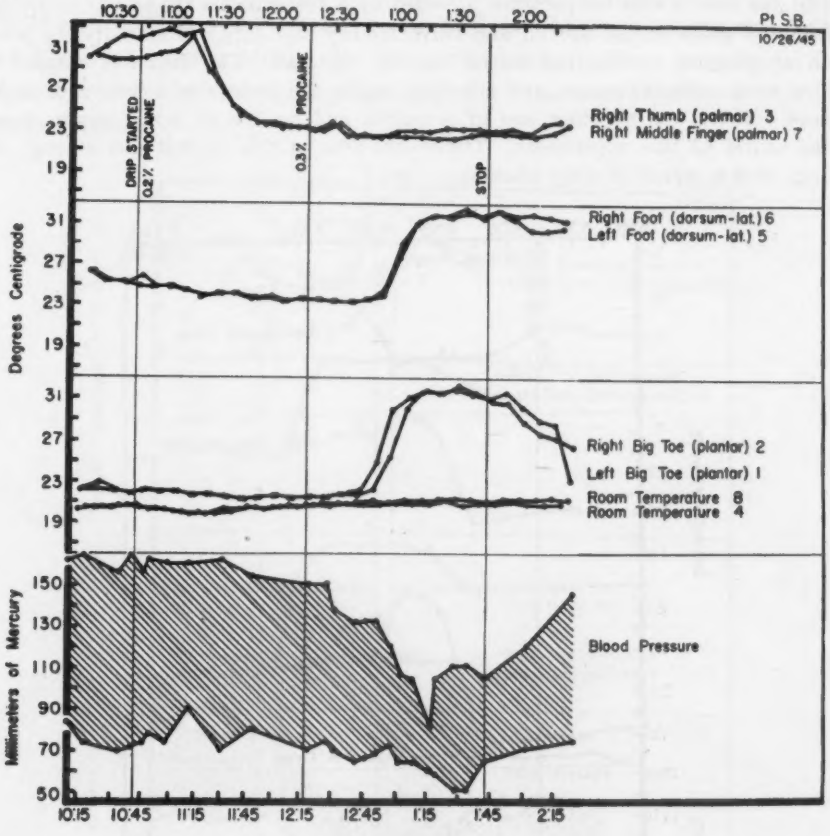

Fig. 4.

CASE 5 (No. 382923).—R. T., 54 years of age, had intractable amputation stump pain (Fig. 5). Only four thermocouples were used in this experiment. Satisfactory skin levels having been obtained, the intraspinal drip of 10 c.c. (20 mg.) of procaine hydrochloride was given in three minutes starting at 5:46 P.M. The drip was then continued at a rate of 15 drops per minute until 7:01 P.M. At 6:15 P.M. the skin temperature of the feet rose sharply and at 6:50 P.M. the skin temperature of the hand (right middle finger) also rose sharply. Impairment of the appreciation of pinprick began to diminish just prior to the rise in skin temperature in the lower extremity. This eventually (6:50 P.M.) rose to the third thoracic segment. Paralleling the rise in skin temperature there was a moderate fall in blood pressure. Slight nausea and vomiting were noted at this time. Accompanying the loss of pinprick and the rise in the skin temperature the patient volunteered that he was experiencing the first relief of the amputation stump pain that he had had for several months. This lasted for three to four hours following the induction of the block. There was no other loss of sensation and no loss of motor power at any time during the course of this experiment. The total dose was 106 mg. in seventy-five minutes.

CASE 6 (No. 509346).—W. S., 53 years of age, had carcinoma of the stomach (preoperative) (Fig. 6). At 2:30 P.M., satisfactory skin temperature levels having been obtained, the initial dose of 10 c.c. (20 mg.) procaine hydrochloride was administered intraspinally in three minutes. At 2:52 P.M. the rate was slowed from 15 drops per minute to 10 drops per minute and this rate was continued until 3:30 P.M. Seven minutes after the initial dose the skin temperature of both feet rose sharply. As the concentration of the drug rose in the upper portion of the spinal canal, complete block became manifest in the upper as well as the lower portion of the thoracolumbar outflow. Paralleling the rise in skin temperature there was a moderate fall in blood pressure which rose again as the skin temperature began to fall. In this patient the rise in skin temperature preceded by a few minutes the loss of appreciation of pinprick in the areas of the second and third lumbar segments. Eventually the loss of appreciation of pinprick rose to the second thoracic segment. The drip was stopped at 3:30 P.M. There were moderate nausea and vomiting during the periods of hypotension and sympathetic block. There was no other loss of sensation and no loss of motor power at any time during the course of this experiment. The initial dose in this patient was 20 mg., the total dose 76 mg., over a period of sixty minutes.

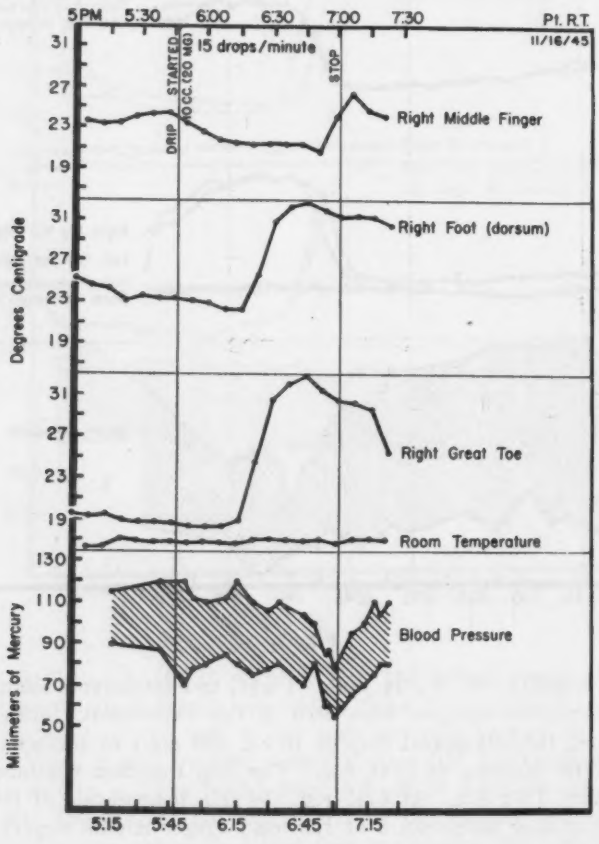

Fig. 5.

Comment.—Cases 5 and 6 demonstrate that it is possible to block not only the lower portion of the thoracolumbar outflow, but the upper portion of the thoracolumbar outflow as well, without blocking sensory fibers other than those concerned with pinprick and without causing motor loss. In Case 6, where there was a complete block of the upper portion as well as the lower portion of the

thoracolumbar outflow, it is justifiable to assume that all the areas in between the upper and the lower portion reacted in the same fashion. In this case, then, we have an experimental preparation in which there are apparently no impulses traveling over the fibers carrying vasoconstrictor impulses to the periphery.

Three patients experienced a loss of sensation to pinprick appreciably before the rise in skin temperature, and the interval between the two end points was long enough to be sure that they were separate phenomena. In two other patients the apparent sympathetic block and the loss of sensation of pinprick came at about the same time. In the sixth patient there was but a circumscribed, minimal loss of pinprick sensation at a time when the lower sympathetic block was complete.

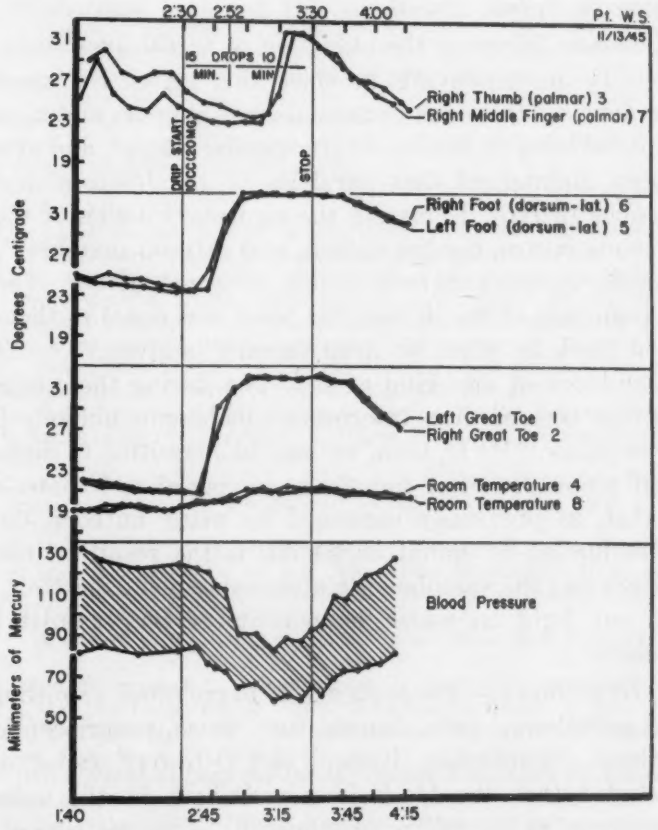

Fig. 6.

Nausea and vomiting were present in four of the six patients studied. These symptoms were absent in two patients, one of whom had a profound fall in blood pressure, in fact, the largest encountered in this series. Nausea and vomiting occurred in one patient in whom the fall in blood pressure was negligible. The pulse rates are not revealing for, although a tachycardia might have been expected in the presence of the low arterial pressure and low filling pressure of the right ventricle and great veins, nevertheless, it is to be assumed

that there is a sufficient amount of procaine high enough in the spinal canal to affect materially the impulses transmitted by the cardiac accelerator fibers. This effectively blocks the reflex activity of the carotid sinus and great veins, the main homeostatic mechanisms under conditions of hypotension. Making this assumption carries with it the implication that cardiac accelerator fibers are blocked by a lower concentration of the agent than the peripheral vasoconstrictor fibers, since a relative bradycardia was present in four patients in whom vasodilatation of the fingers did not occur.

A differential spinal block was given to twenty-four additional patients; the findings did not differ materially from those of the six described in this paper. The details of these twelve cases will be given in a later communication in which the use of the method in diagnosis and therapy is described.[22]

Hypotension in Spinal Anesthesia.—It has been suggested[12, 13, 14] that the fall in blood pressure following the induction of spinal anesthesia is due to the muscular flaccidity accompanying it, since this leaves the vascular bed unsupported and deprives the veins of their normal support and massaging action, with consequent lowering of venous return, cardiac output, and arterial pressure. It has also been maintained that paralysis of the intercostal muscles limits thoracic excursions thereby decreasing the aspiratory action of the thorax, thus diminishing venous return, cardiac output, and arterial pressure.[13, 14, 15] In our group of patients sympathomimetic drugs were not given. The hypotension following the induction of the differential block was equal to that seen with the undifferentiated block in which no drug therapy is given.[12, 16] Yet we did not encounter motor block of any kind at any time during these experiments, and it would seem that both of these interpretations become unlikely in the light of this and other evidence.[16-19] If, then, we may be permitted to discard the loss of appreciation of pinprick as not significant in regard to hypotension, it would seem certain that, as previously suggested by many authors, the hypotension following the induction of spinal anesthesia is the result of the paralysis of sympathetic fibers and the vascular dilatation consequent thereto. This evidence does not shed any light on which components of the vascular bed are most directly responsible.

Order of Nerve Block.—The sequence of nerve block according to Maxson[20] and Evans[21] is as follows: pain, temperature, touch, proprioception, motor and sympathetic fibers. Heinbecker, Bishop, and O'Leary,[3] using more definitive methods, concluded that the block of nerves both in the spinal canal and peripherally occurred in the following sequence: vasoconstrictors, temperature, pain, motor, joint sense, pressure sense, and touch. By slowing down the sequence of events as they occur, with the use of a dilute solution, we are able to bring a finer focus to bear on this sequence. It will be seen from the cases which we have presented and from research now in progress that there is no single regular sequence of events but that either the sympathetic fibers or the fibers concerned with the appreciation of pinprick may be blocked first, occasionally as much as forty-five minutes occurring between the block of the two kinds of fibers.

SUMMARY AND CONCLUSIONS

1. It is possible to introduce a concentration of procaine into the subarachnoid space which will block the fibers carrying vasoconstrictor impulses to the periphery and also those concerned with pinprick without materially affecting fibers concerned with touch, proprioception, vibratory sense, or motor power. This is termed differential spinal block.

2. Hypotension during spinal anesthesia is not the result of muscular flaccidity or diminished thoracic excursions but is a result of the interruption of sympathetic vasoconstrictor fibers.

3. The determination of the level of the loss of sensation to pinprick yields only very approximate information concerning the level of block of other kinds of fibers.

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Review of Recent Meetings

ANNUAL MEETING OF THE SOCIETY OF UNIVERSITY SURGEONS

NEW YORK, N. Y., FEB. 7-9, 1946

CLARENCE DENNIS, M.D., MINNEAPOLIS, MINN.

THE 1946 meeting of the Society of University Surgeons was held in New York, N. Y., Feb. 7, 8, and 9, 1946; members were guests of the surgical staff of the Columbia-Presbyterian Medical Center. The group was welcomed by **Dean Rappleye**, who pointed out two challenges to be met by groups such as this: The first, that of surgical training for the returning servicemen, and the second, the maintenance of high surgical standards in the face of the prepayment medical plans shortly to be instituted.

Dr. Whipple related his experiences in surgical extirpation of pancreatic cancers, with his conclusions on proper diagnostic and technical procedures. **Dr. Darrach** discussed the history of the Lane technique in the plating of fractures and **Dr. Auchincloss** spoke of Dupuytren's contraction. **Dr. St. John** presented his much-discussed data on the frequency of discovery of gastric malignancies in routine gastrointestinal roentgen studies of patients past 50 years of age (1.24 per 1,000). **Dr. Golden** presented roentgen evidence that the occasional occurrence of vomiting after gastrectomy is due to marked temporary hypertonicity in the proximal and distal loops. **Dr. Canavarro** presented some of the first statistically significant data to appear in support of early ambulation after surgery. In 500 cases, as compared to 500 controls, postoperative complications were cut in half by early ambulation, less medication was needed, patient morale was better, and savings in cost and hospital bed days resulted. Patients were made to walk within twenty-four hours. **Dr. Richards** presented results on catheterization of the heart via the basilic vein, with data on lesser circuit pressures in various cardiac and pulmonary diseases. **Dr. Humphreys** presented a case of pulmonic stenosis improved by the Blalock operation. **Dr. McDonald** presented a very convincing film on the use of heterologous skin grafts as temporary dressings in extensive burns. **Dr. Hanger** presented a readily comprehensible arrangement of tests of liver function—one that seemed to simplify the problem to most members. **Dr. Seegal** aroused much interest and speculation by her presentation of the isolation and antibiotic activity of protoanemonin, a derivative from buttercups; this agent is effective against *Bacillus coli* and the tubercle bacillus in doses well tolerated experimentally. **Dr. Frantz** presented data on her absorbable gauze for hemostasis. Finally, **Dr. Parsons** made a plea that returning members of the Armed Services keep their reserve commissions and otherwise retain an active interest in the medical departments to avoid repetition of errors of the early period of World War II.

During the afternoon of February 7, members of the Columbia-Presbyterian staff presented further brief reports. **Dr. Moore** presented reasons for quick aspiration of traumatic hemothorax without air replacement. **Dr. Haagensen** showed statistics indicating education of both the public and the profession in the next step in reduction of breast cancer mortality. **Dr. Werner** reported intravenous use of crystallized amino acids, and **Dr. McLaughlin** discussed the use of removable wire sutures in tendon repairs. Experiences with thiouracil were recounted by **Dr. Elliott**; 20 per cent of the patients in his series developed complications, but the drug seemed more valuable than iodine alone. **Dr. Maier** dwelt on bronchogenic cysts and methods of diagnosis.

A series of demonstrations by members of the Columbia-Presbyterian staff, **Doctors Frantz, Meleney, Scudder, Murray, Howes,** and **Blakemore** completed the sessions for the first day.

Papers presented by visiting members of the Society are to be found elsewhere in this issue of SURGERY.

The Columbia-Presbyterian group left a very marked impression upon the members of the Society because of the quality and quantity of the investigative work being pursued there. From quite another vantage point the impression was equally marked, for in addition to the scheduled cocktail hour, the formal dinner at the Pennsylvania Hotel, and the excellent luncheons served to the guests, the group proved cordial hosts on every occasion throughout the meeting.

Book Reviews

Plaster of Paris Technique. By T. B. Quigley, M.D. Pp. 107. New York, 1945, The Macmillan Company.

This monograph is a well-written manual dealing with the practical application of plaster casts. It is well illustrated with photographs which for the most part show the steps in the application of casts to the various parts of the body. The description of improvised methods of supporting patients for application of hip spicas and other casts is good and the methods are unique.

Since this is a manual designed to instruct those unfamiliar with the use of plaster and the application of casts, only a single, simple method is described in most cases. One might gain the impression that fracture tables and more conventional methods of applying casts are unnecessary and not needed.

As a whole the monograph is sufficiently complete and covers the necessary material well. It should find its place as a supplementary text in the medical student's library and as a manual for all interns, residents, and practitioners who must apply casts.

General and Plastic Surgery, With Emphasis on War Injuries. By J. Eastman Sheehan, M.D., Professor of Plastic Reparative Surgery, New York Polyclinic Medical School and Hospital. Pp. 345, with 495 illustrations. New York, 1945, Paul B. Hoeber, Inc. $6.75.

This brief text outlines a number of well-known principles in the treatment of war wounds. The earlier chapters comment rather generally on the principles of wound excision, control of infection, and the various types of wounds resulting from war trauma.

The chapters on burns are quite brief. The illustrations throughout the book are almost entirely copied from other texts, particularly from Hamilton Bailey's writings.

The latter chapters deal with the regions of the body and describe a number of standard plastic procedures.

Fractures of the Jaws. By Robert H. Ivy, M.D., D.D.S., F.A.C.S., and Lawrence Curtis, A.B., M.D., D.D.S., F.A.C.S., University of Pennsylvania. Ed. 3. Pp. 174, with 199 illustrations. Philadelphia, 1945, Lea & Febiger. $4.50.

This, the third edition of this popular book, maintains the high standards set by the previous editions. The authors draw their material from a large experience with the subject and the excellent drawings and illustrations are nearly all from their own cases. The book is well written and the different types of fractures are dealt with clearly and concisely. There are, in addition, chapters on the Roentgenographic Technique and Dietary Management in Jaw Fractures. This book is a valuable contribution not only for the oral surgeon but for the general surgeon as well.

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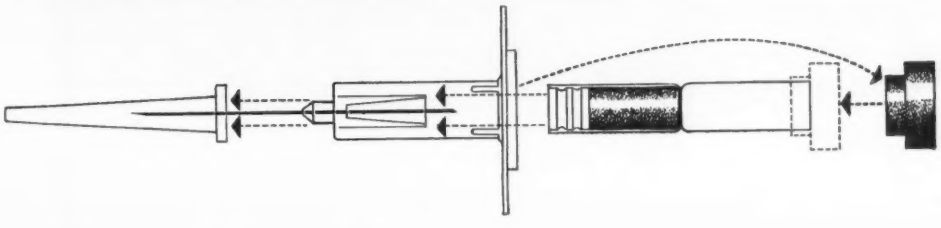

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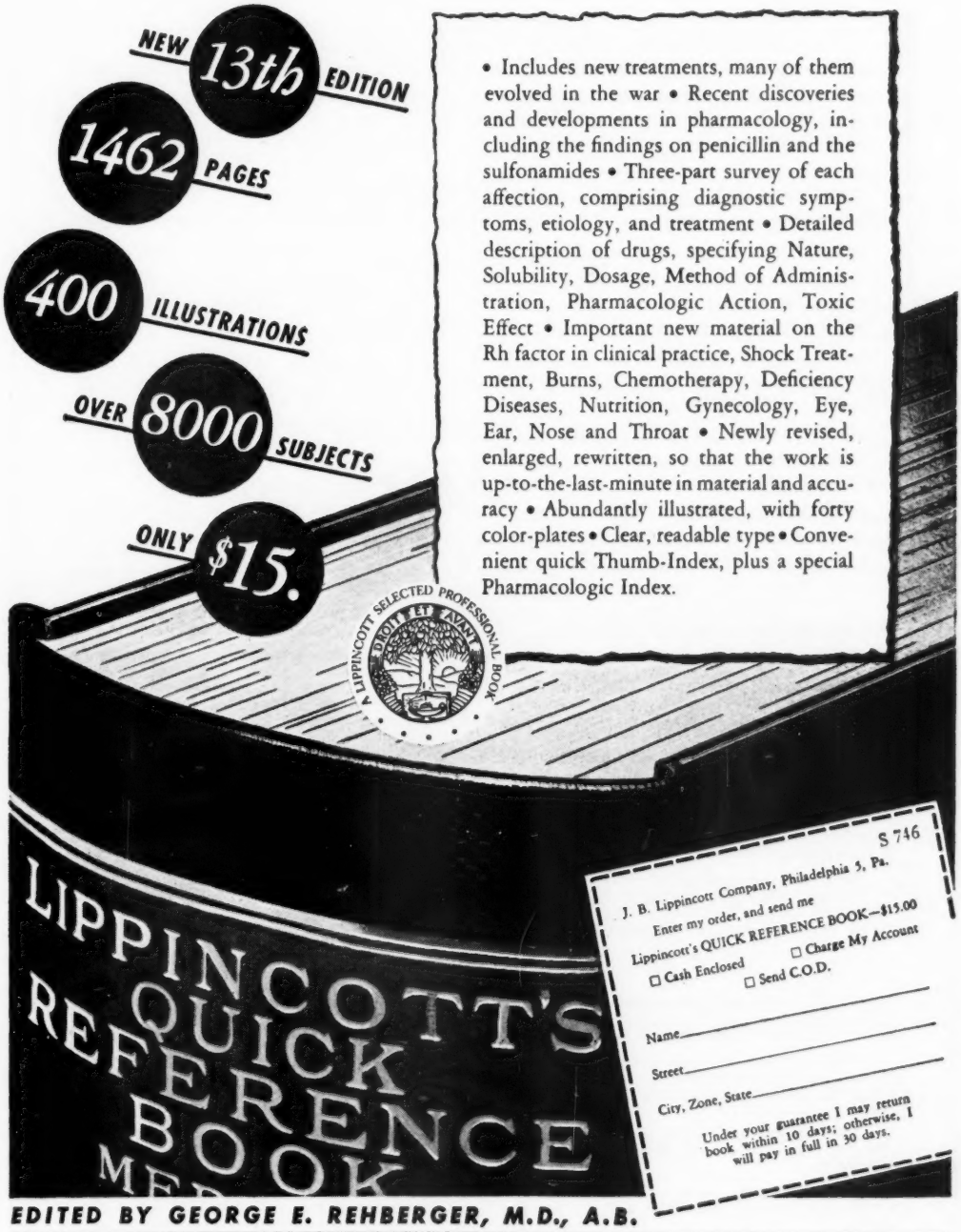

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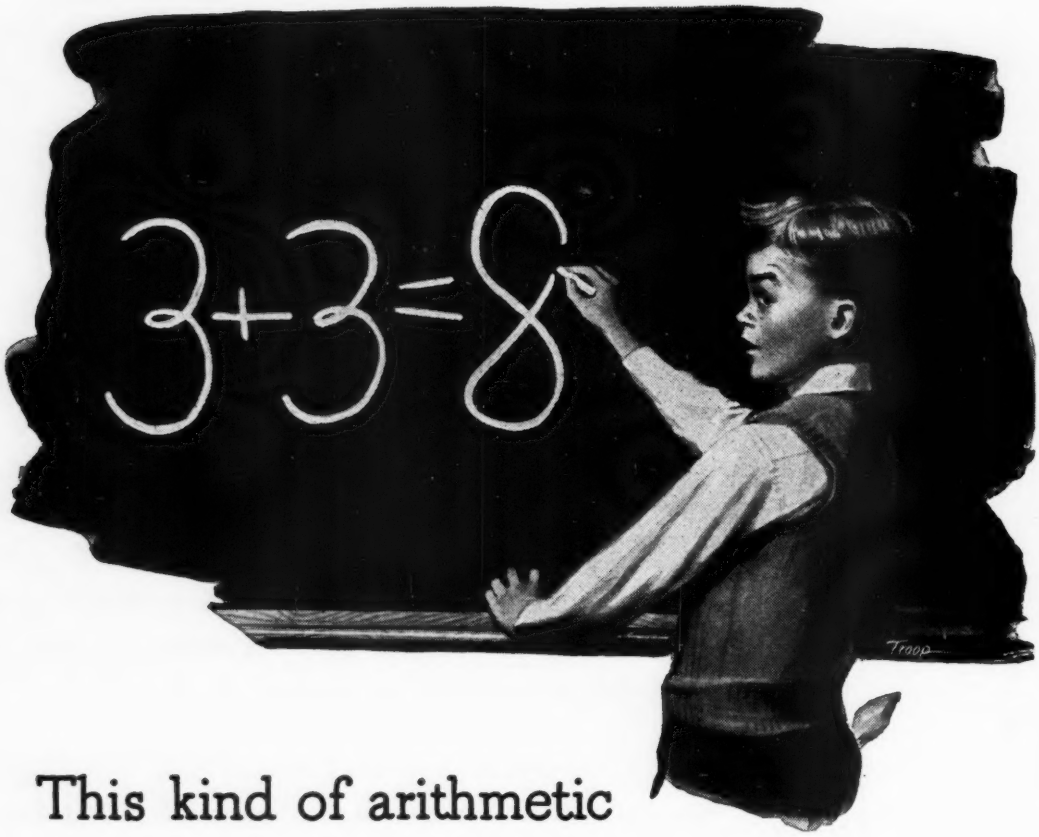

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